SEHSC
SILICONES ENVIRONMENTAL, HEALTH AND SAFETY COUNCIL
NORTH AMERICA

Phone: 703 788 6570
Fax: 703 788 6545
www.sehsc.com
2325 Dulles Corner Boulevard
Suite 500
Herndon VA 20171

December 7, 2007
Via Certified Mail

MR # 3-8503

TSCA Confidential Business Information Center (7407M)
EPA East – Room 6428
Attn: TSCA Section 8(e) Coordinator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Contain NO CBI

Re: Supplemental TSCA Section 8(e) Submission; Final Report - 2-Butanone, O,O',O"– (methylsilylidyne)trioxime: 7-Day Range-Finding Oral Toxicity (Gavage) Study in the Rat

Dear TSCA Section 8(e) Coordinator:

The Silicones Environmental, Health and Safety Council of North America (SEHSC)[1], on behalf of its member companies, is submitting the enclosed final report, "2-Butanone, O,O', O" – (methylsilylidyne) trioxime: 7-Day Range-Finding Oral Toxicity Study of in the Rat: RCC Ltd. Study Number: 857737" as a supplemental submission to our August 21, 2007, TSCA Section 8(e) notification. On August 21, 2007, SEHSC provided EPA with preliminary results of the referenced study in accordance with the provisions of section 8(e) of the Toxic Substances Control Act (TSCA). This final report is being provided for the Agency's reference. Neither SEHSC, nor any member company, has made a determination at this time that any significant risk of injury to human health or the environment is presented by the report's findings.

Chemical Substance

22984-54-9	2-Butanone, O, O', O" – (methylsilylidyne) trioxime Methyltris(methyl ethyl ketoxime)silane (additional name)

Final Study Report

2-Butanone, O,O', O" – (methylsilylidyne) trioxime: 7-Day Range-Finding Oral Toxicity Study of in the Rat: RCC Ltd. Study Number: 857737

Summary

Results of a 7-day range finding study conducted with 2-Butanone, O,O',O" – (methylsilylidyne) trioxime in Wistar rats show indications of treatment-related effects. All treated animals had enlarged and statistically significantly increased mean absolute and relative spleen weights. Animals in the 1000 mg/kg dose group exhibited signs of sedation, ventral recumbancy, ruffled fur, uncoordinated movements, hunched posture, and a bluish appearance of paws. Animals in the 500 mg/kg exposure group exhibited sedation, ventral recumbancy, ruffled fur, and

[1] SEHSC is a not-for-profit trade association whose mission is to promote the safe use of silicones through product stewardship and environmental, health and safety research. The Council is comprised of North American silicone chemical producers and importers.

RCC Study Number: 857737

2-Butanone, O,O',O''-(methylsilylidyne) trioxime

7-Day Range-Finding Oral Toxicity (Gavage) Study in the Rat

Report

Authors

Dr. R. Gerspach, Dr. D. Flade

uncoordinated movement. In female animals in the 500 mg/kg and 1000 mg/kg exposure group, the mean relative liver weight was also statistically significantly increased.

2-Butanone, O,O',O" – (methylsilylidyne) trioxime releases methyl ethyl ketoxime (MEKO) upon contact with humid air or water. Results reported in the current study are consistent with those reported for exposure to MEKO.

Details

Study Design

The objective of this study was to evaluate the potential toxicity of 2-Butanone, O,O',O" – (methylsilylidyne) trioxime in Wistar rats following oral gavage exposure in preparation of dose level selection for a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Screening Test (OECD 422).

Groups of 4 male and 4 female HanRcc:WIST(SPF) rats were administered the test article, 2-Butanone, O,O',O" – (methylsilylidyne) trioxime, once daily for seven consecutive days by oral gavage. Dose levels were 250, 500, and 1000 mg/kg/day. A concurrent control group was dosed with corn oil vehicle alone. The dosage volume for all groups was 2 mL/kg. Oral ingestion is not an intended route of exposure; however, it is an acceptable route of exposure for evaluating the potential toxicity of a material.

All animals were observed twice daily for appearance and behavior. Clinical observations, body weights, and food consumption were recorded at appropriate intervals. All animals were sacrificed at the end of the 7-day dosing period. All macroscopic observations were recorded and selected organs from the animals were weighed. Data were analyzed using appropriate statistical tests.

Results

Clinical Observations

At 1000 mg/kg/day, all animals showed sedation, ventral recumbency, ruffled fur, uncoordinated movements, hunched posture, and blueish appearance of paws. To a lesser extent, animals in the 500 mg/kg/day dose group exhibited sedation, ventral recumbency, ruffled fur, and uncoordinated movements.No clinical signs were noted in animals exposed to 250 mg/kg/day.

Body Weights

A dose dependent decrease in body weight gain was noted in all test article-treated groups. Overall the mean body weight gain was decreased by 30 and 70% in males and by 22 and 56% in females of groups 2 and 3, respectively. In 1000 mg/kg/day group, animals either lost weight (males -5%) or did not gain weight (females).

Food Consumption

A dose-dependent decrease in food consumption was observed in all test article-treated groups. The mean food consumption was decreased by 16, 33 and 55% in

males and by 5, 15 and 38% in females of groups 2, 3 and 4, respectively when compared to control values.

Organ Weights

Spleen weight was statistically significantly increased in all treated animals. At 1000 mg/kg/day, mean absolute spleen weights were increased 311% (n=4) in males and 358% (n=4) in females. At 500 mg/kg/day, mean absolute spleen weights were increased 342% (n=4) in males and 404% (n=4) in females. At 250 mg/kg/day, mean absolute spleen weights were increased 270% (n=4) in males and 304% (n=4) in females. The spleen was identified as the target organ in this study. In 1000 mg/kg/day group, 2 males had enlarged, reddish mesenteric lymph nodes and one had reddish discolored lymph nodes. In female animals in the 500 and 1000 mg/kg/day groups, the mean relative liver weight was also statistically significantly increased.

Additional Information

This material releases methyl ethyl ketoxime (MEKO) upon contact with humid air or water. The health hazards associated with exposure to MEKO have been well characterized and the Agency has been notified of these findings by other submitters. Numerous toxicological studies have been performed on MEKO and the health effects observed in these studies include increases in spleen weight, central nervous system (CNS) depression, hemolytic effects, and skin sensitization. Results reported in the current study are consistent with those reported for exposure to MEKO (TOMES; RTECS; Honeywell MSDS for Methyl Ethyl Ketoxime).

If you have any questions regarding this submission, please contact me at (703) 788-6570, rmenning@sehsc.com, or at the address provided h[redacted]

Sincerely,

Reo Menning
Executive Director

Enclosure

Table of Contents

1 PREFACE

1.1 GENERAL

Title	2-Butanone, O,O',O''-(methylsilylidyne) trioxime: 7-Day Range-Finding Oral Toxicity (Gavage) Study in the Rat
Sponsor	SEHSC 2325 Dulles Corner Boulevard Suite 500 Herndon VA 48611 USA
Study Monitor	Waheed H. Siddiqui, Ph.D. Dow Corning Corporation 2200 West Salzburg Road Auburn, MI 48611 / USA
Study Director	Dr. R. Gerspach RCC Ltd Safety Assessment Toxicology I Wölferstrasse 4 CH-4414 Füllinsdorf / Switzerland
Test Facility	a) RCC Ltd CH-4414 Füllinsdorf / Switzerland
Test Site	b) RCC Ltd CH-4452 Itingen / Switzerland

1.2 RESPONSIBILITIES

Study Director	Dr. R. Gerspach (a)
Deputy Study Director	Dr. A. Poessnecker (a)
Technical Coordinators	D. Frei, H. Perez (a)
Principal Investigator: Study Phase: Analytical Chemistry	Dr. D. Flade (b)

1.3 SCHEDULE

Delivery of Animals	24-JAN-2007
Acclimatization Start	24-JAN-2007
Treatment Start	31-JAN-2007
Termination/Necropsy	07-FEB-2007

1.4 ANIMAL WELFARE

This study was performed in an AAALAC-approved laboratory in accordance with the Swiss Animal Protection Law under license No. 252.

1.5 SUMMARY OF STUDY PLAN AMENDMENT

First Amendment	Change of Sponsor's address.
	The test item Batch number 041201 was used, due to technical error. As specification of the batch is appropriate, this does not jeopardize the validity of the study.

1.6 ARCHIVING

RCC Ltd (CH-4452 Itingen/Switzerland) will retain the study plan, study plan amendment, raw data, sample of test item(s), specimens (as long as the quality permits evaluation) and the final report of the present study, the phase report and raw data of test site for at least ten years. Wet tissue samples will be archived at RCC Ltd for a minimum of five years. Thereafter, in agreement with the Sponsor, these samples may be further archived at RCC Ltd or transferred to another GLP archive facility for the remainder of the prescribed period. No data will be discarded without the Sponsor's written consent.

1.7 SIGNATURES

STUDY DIRECTOR: Dr. R. Gerspach

.....
date: October 30, 2007

DEPUTY STUDY DIRECTOR: Dr. A. Poessnecker

.....
date: 30-OCT-2007

TEST FACILITY MANAGEMENT: (fa) Dr. H. Fankhauser

.....
date: 30-OCT-2007

2 SUMMARY

The purpose of this toxicity range-finding oral study was to assess the toxicological profile of the test item when administered daily to rats by oral gavage for a period of 7 days.

This study should provide a rational basis to select the dose levels for subsequent oral toxicity studies.

The following dose levels were applied:

Group 1: 0 mg/kg body weight/day (vehicle control)
Group 2: 250 mg/kg body weight/day
Group 3: 500 mg/kg body weight/day
Group 4: 1000 mg/kg body weight/day

The test item was administered once daily orally (by gavage) to male and female rats for 7 days. A standard dose volume of 2 mL/kg body weight with a daily adjustment to the actual body weight was used. Control animals were dosed with the vehicle alone (dried corn oil). Clinical signs, food consumption and body weights were recorded. On day 8 of treatment, animals were sacrificed, and organ weight measurements were performed. Macroscopical changes were recorded.

The following results were obtained:

MATERNAL DATA

General Tolerability

No deaths occurred. In the 1000 mg/kg body weight/day dose group all animals showed sedation, ventral recumbency, ruffled fur, uncoordinated movements, hunched posture, and bluish appearance of paws. To a lesser extent, sedation, ventral recumbency, ruffled fur, and uncoordinated movements were noted at 500 mg/kg body weight/day.

There were no clinical signs in group 2 (250 mg/kg body weight/day).

Food Consumption and Body Weights

There was a dose-dependent decrease in food consumption in all test item-treated groups. Overall (treatment days 1 - 8), the mean food consumption was decreased by 16%, 33%, and 55% in male groups 2, 3, and 4, respectively, and by 5%, 15%, and 38% in female groups 2, 3, and 4, respectively, compared with the respective control group value.

Retarded body weight development was noted in all test item-treated groups. Overall (treatment days 1-8), the mean body weight gain was decreased by 30% and 73% in male groups 2, and 3, respectively, and by 22% and 56% in female groups 2, and 3, respectively, compared with the respective control group value. In group 4, animals even lost weight (males -5%) or did not gain weight (females).

Necropsy Findings

In all test item-treated groups, all males and all females had enlarged spleens. In group 4, 2 males had enlarged, reddish mesenteric lymph nodes, and one had reddish discolored lymph nodes.

Organ Weights

In all test item-treated groups, the mean absolute and relative spleen weights were markedly and statistically significantly increased. In addition, in female groups 3 and 4, the mean relative liver weight was statistically significantly increased.

3 CONCLUSION

In this 7-day range finding study in rats, oral treatment with the test item caused overt toxicity at the 1000 and 500 mg/kg body weight/day dose levels. Occurrence of clinical signs, as well as decreases in of food consumption and body weight gain indicated that the Maximum Tolerated Dose was exceeded at these dose levels. Strongly increased spleen weights occurred in all dose groups. Enlarged spleens were noted in all treatment groups.

4 PURPOSE AND RATIONALE

The purpose of this oral toxicity range-finding study was to assess the toxicological profile of the test item when administered daily to rats by oral gavage for a period of 7 days.

This study will be used to select the dose levels for subsequent oral toxicity studies.

5 MATERIALS AND METHODS

General Remark: Details of the materials and methods that are not specified in the subsequent sections of this report are contained in the appropriate RCC standard operating procedures.

5.1 TEST SYSTEM

Species	Rat, HanRcc:WIST (SPF)
Rationale	Specified by the international guidelines as the recommended test system
Source	RCC Ltd Laboratory Animal Services Wölferstrasse 4 CH-4414 Füllinsdorf / Switzerland
Number of animals	16 males, 4 per group 16 females, 4 per group
Age at delivery	10 weeks
Body weights (at first treatment)	Males: 307 - 335 grams Females: 191 - 216 grams
Acclimatization	Five days (minimum) under test conditions with an evaluation of the health status
Identification	Individual animal number tattooed on the pinnae and individual cage card

5.2 HUSBANDRY

Facility	Animals were housed at RCC Ltd, Füllinsdorf
Room number	008A
Conditions	The study was performed under standard laboratory conditions: the animal room was air-conditioned with 10-15 air changes per hour; the environment was monitored continuously with recordings of temperature (range 22 ± 3°C) and relative humidity (range 30-70%), 12 hours artificial fluorescent light / 12 hours dark with background music played at a centrally defined low volume for at least 8 hours during the light period.
Accommodation	Animals were housed individually in Makrolon cages (type-3) with wire mesh tops and standard granulated softwood bedding (Lignocel, Schill AG, CH-4132 Muttenz/ Switzerland). Throughout the study, each cage was identified by a colored label according to the group and recording the study schedule number, animal number(s) and details of treatment.
Diet	Pelleted standard Kliba-Nafag 3433 rat/mouse maintenance diet (Provimi Kliba AG, CH-4303 Kaiseraugst / Switzerland) was available *ad libitum* (Batch No. 67/06). Results of analyses for contaminants are presented in Attachment I.
Water	Tap water from Füllinsdorf from an automatic system was available *ad libitum*. Results of the bacteriological, chemical and contaminant analyses scheduled to be conducted at least once yearly by RCC (contaminant analyses only) and by the Official Chemist of the Kanton Basel-Landschaft (bacteriological and chemical analyses) are presented in Attachment II.

5.3 TEST ITEM

Test item and test item data were obtained from Honeywell and the Sponsor (see Attachment III).

Identity	2-Butanone, O,O',O''-(methylsilylidyne) trioxime
Synonyms	OS-1000; methyl oximino silane
Cas No.	22984-54-9
Batch Number	041201
Description	Clear colorless liquid

Purity (G.C.)	96.1%
Expiration date	01-DEC-2009
Stability in the vehicle	At least 7 days (according to the results of the validation study RCC 858728).
Instruction for test item storage	At room temperature in closed containers under nitrogen atmosphere
Safety precautions	Routine hygienic procedures were applied to ensure personnel security.

The test item was also used as the analytical standard for analysis of dose formulations.

5.4 VEHICLE AND CONTROL ITEM

Identity	Dried corn oil (certificate of analysis is presented in Attachment III)
Supplier	Carl Roth GmbH & Co., D-76185 Karlsruhe/Germany
Batch number	05566202
Expiration date	12-MAR-2007
Storage conditions	At room temperature (20 ± 5°C)
Safety precautions	Routine hygienic procedures (gloves, goggles, face mask)

5.5 DOSE FORMULATION

Dose levels were in terms of test item as supplied. No corrections were performed on the dose levels based on either the density or purity of the test item.

The test item was administered in the specified vehicle (dried corn oil). Mixtures of the test item in the vehicle (weight : volume) at appropriate concentrations were performed once.

Homogeneity of the test item in the vehicle was maintained during the daily administration period using a magnetic stirrer.

Frequency of dose formulation	once weekly, according to the results of the validation study (RCC 858728).
Storage of dose formulations	at 5±3°C (according to the results of the validation study RCC 858728), under nitrogen atmosphere.

5.5.1 ANALYSIS OF DOSE FORMULATIONS

Samples for determination of actual test item concentrations, stability (7 days) and homogeneity in the prepared mixtures were taken on the first day of preparation. Samples of each dose concentration were taken before dosing (from the top, middle and bottom of the container). Later, samples were taken from the middle of the container for verification of stability at 5±3°C for 7 days. Samples were stored in measuring flasks at -20 °C ± 5 °C. A sample of approximately 2 g of vehicle was taken. Samples and approximately 2 g of the test item were transported frozen to RCC Ltd, Environmental Chemistry & Pharmanalytics, CH-4452 Itingen/Switzerland.

Analyses were performed using a method developed by RCC Ltd, Environmental Chemistry & Pharmanalytics: Gas Chromatographic (GC). After analysis the analytical results were communicated to the Study Monitor as soon as practically possible. Upon receipt of these analytical results the Study Monitor was given an opportunity to review and discuss these analytical results with the PI. Once any concerns of the Study Monitor had been addressed by the PI, the dose formulation samples were discarded at the discretion of the PI for the Analytical Phase. The results of the Analytical Phase are presented in Attachment IV.

5.6 ALLOCATION

Group	Male Numbers	Female Numbers	Dose mg/kg/day
1	1 - 4	17 - 20	0 (vehicle control)
2	5 - 8	21 - 24	250
3	9 - 12	25 - 28	500
4	13 - 16	29 - 32	1000

Method of allocation

Prior to start of the acclimatization period, animals were assigned to the different groups using a computer-generated random algorithm. In addition, body weights (recorded on the day of allocation) were taken into consideration in order to ensure similar mean body weights in all groups.

Administration

After acclimatization, animals of both sexes received the test item for seven days. The test item was administered orally, by gavage, once daily. All animals received a dose volume of 2 mL/kg body weight with a daily adjustment of the individual volume to the actual body weight. Control animals were dosed with the vehicle alone.

Rationale for route of administration

Oral ingestion is not an intended route of exposure, however it is an accepted route of exposure for this type of study.

5.7 OBSERVATIONS

Mortality rate

All animals were checked at least twice daily for any mortalities. All rats found dead were subjected to a detailed macroscopic examination to establish, if possible, the cause of death.

Signs and/or symptoms

All animals were observed at least twice daily for signs of reaction to treatment and/or symptoms of ill health.

Food consumption

Food consumption was reported for the following periods: during acclimatization: days 1 - 3, 3 - 5 and 5 - 7 and during treatment days 1 - 3, 3 - 5 and 5 - 7.

Body weights

Body weights were recorded daily.

5.8 PATHOLOGY

5.8.1 NECROPSY

All animals were weighed and necropsied. Descriptions of all macroscopic abnormalities were recorded. All animals surviving to the end of the observation period were killed by CO_2.

5.8.2 ORGAN WEIGHTS

The weights of the following organs were recorded for all animals on the scheduled date of necropsy:

Uterus	Ovaries	Testes	Epididymides
Prostate	Seminal vesicles	Liver	Kidneys
Spleen			

5.9 STATISTICAL ANALYSIS

The following statistical methods were used to analyze the body weight, food consumption, organ weights and all ratios:

- If the variables could be assumed to follow a normal distribution, the Dunnett-test (many to one t-test) based on a pooled variance estimate was applied for the comparison of the treated groups and the control groups for each sex.
- The Steel-test (many-one rank test) was applied instead of the Dunnett-test when the data could not be assumed to follow a normal distribution.
- Fisher's Exact test for 2x2 tables was applied if the variables could be dichotomized without loss of information.

References :

- C.W. Dunnett: A Multiple Comparison Procedure for Comparing Several Treatments with a Control, J. Amer. Stat. Assoc. 50, 1096-1121 (1955).
- R.G. Miller: Simultaneous Statistical Inference, Springer Verlag, New York (1981).
- R. A. Fisher Statistical Methods for Research Workers, Oliver and Boyd, Edinburgh (1950)

6 RESULTS

6.1.1 MORTALITIES AND/OR SIGNS OF REACTION TO TREATMENT

(pp. 43 , 105)

All animals survived to the scheduled termination. In group 4 (1000 mg/kg body weight/day) all animals showed sedation, ventral recumbency, ruffled fur, uncoordinated movements, hunched posture, and bluish appearance of paws. To a lesser extent, sedation, ventral recumbency, ruffled fur, and uncoordinated movements were noted in group 3 (500 mg/kg body weight/day).

There were no clinical signs in group 2 (250 mg/kg body weight/day).

6.1.2 FOOD CONSUMPTION

(pp. 17 , 31 , 56 , 23 , 37 , 80)

A dose-dependent decrease in food consumption was observed in all test item-treated groups. Overall (treatment days 1 - 8), the mean food consumption was decreased by 16%, 33%, and 55% in male groups 2, 3, and 4, respectively, and by 5%, 15%, and 38% in female groups 2, 3, and 4, respectively, compared with the respective control group value.

6.1.3 BODY WEIGHTS

(pp. 19 , 33 , 64 , 25 , 39 , 88)

A dose-dependent decrease in body weight gain was noted in all test item-treated groups. Overall (treatment days 1 - 8), the mean body weight gain was decreased by 30% and 73% in male groups 2, and 3, respectively, and by 22% and 56% in female groups 2, and 3, respectively, compared with the respective control group value. In group 4, animals even lost weight (males -5%) or did not gain weight (females).

6.1.4 NECROPSY FINDINGS

(pp. 48 , 113)

In all test item-treated groups, all males and all females had enlarged spleen. In group 4, 2 males had enlarged, reddish mesenteric lymph nodes, and one had reddish discolored lymph nodes.

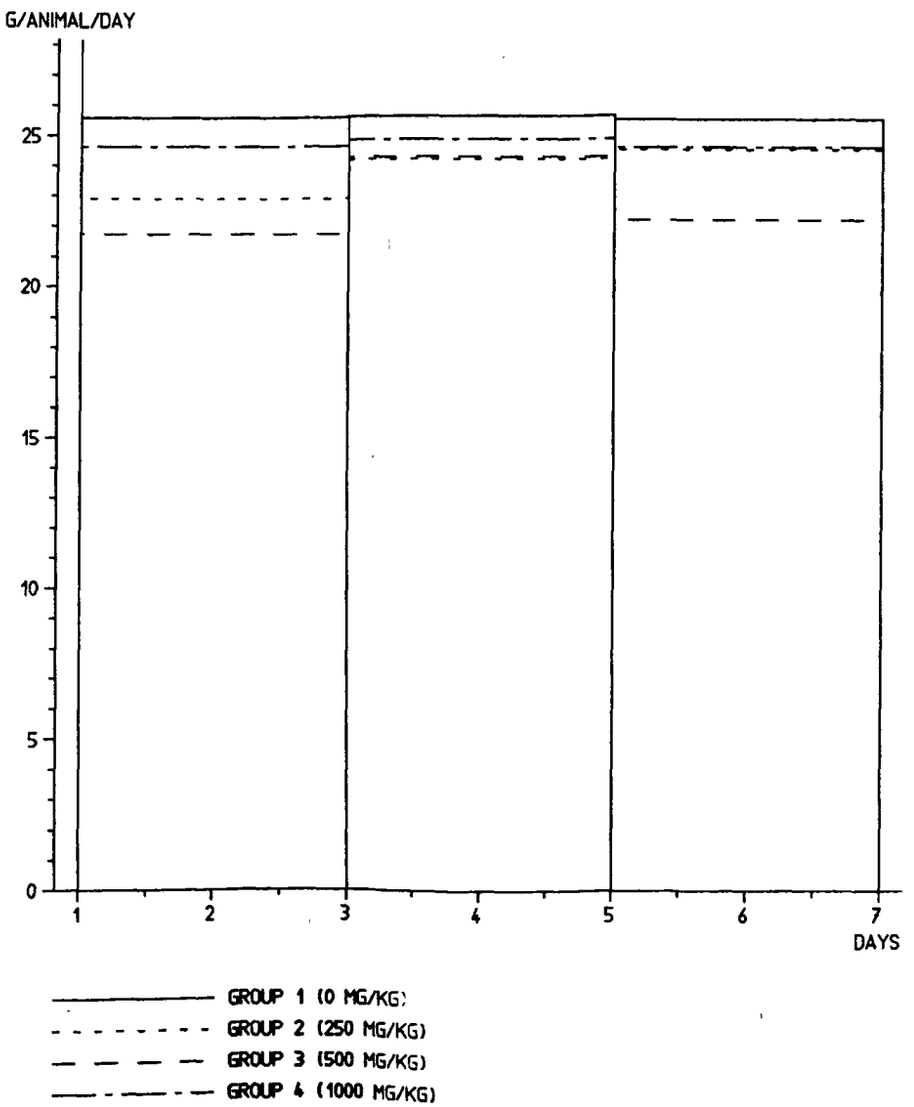
6.1.5 ORGAN WEIGHTS

(pp 50 , 121)

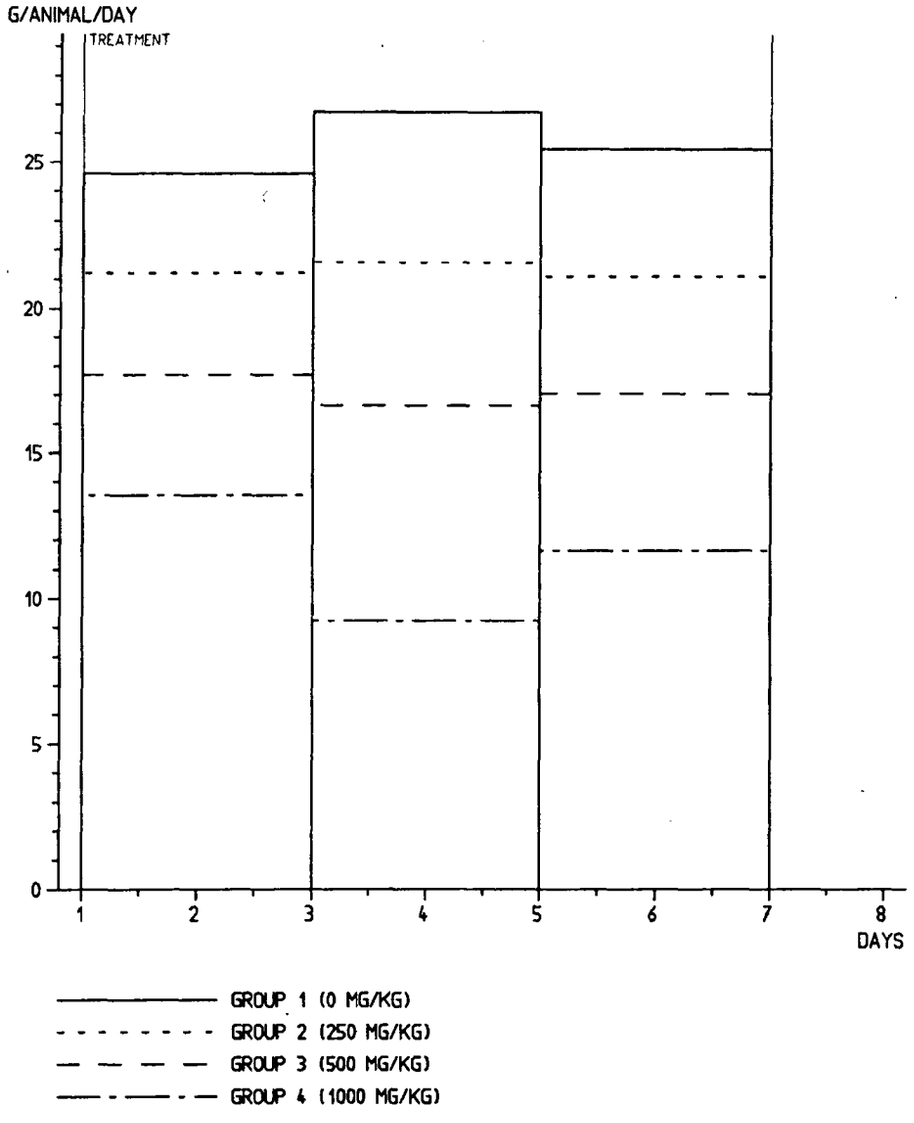
In all test item-treated groups, the mean absolute and relative spleen weights were markedly and statistically significantly increased. In addition, in female groups 3 and 4, the mean relative liver weight was statistically significantly increased.

7 FIGURES

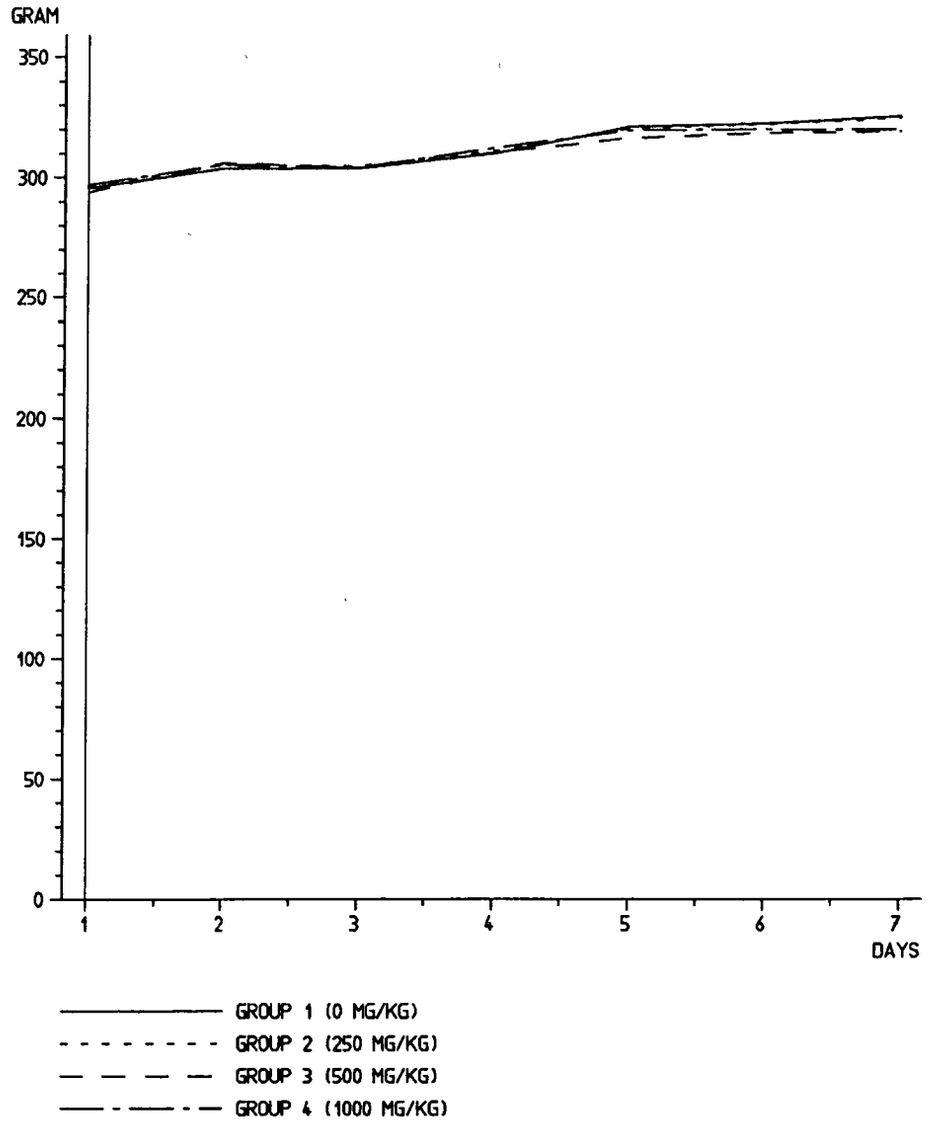
FOOD CONSUMPTION OF MALES
ACCLIMATIZATION



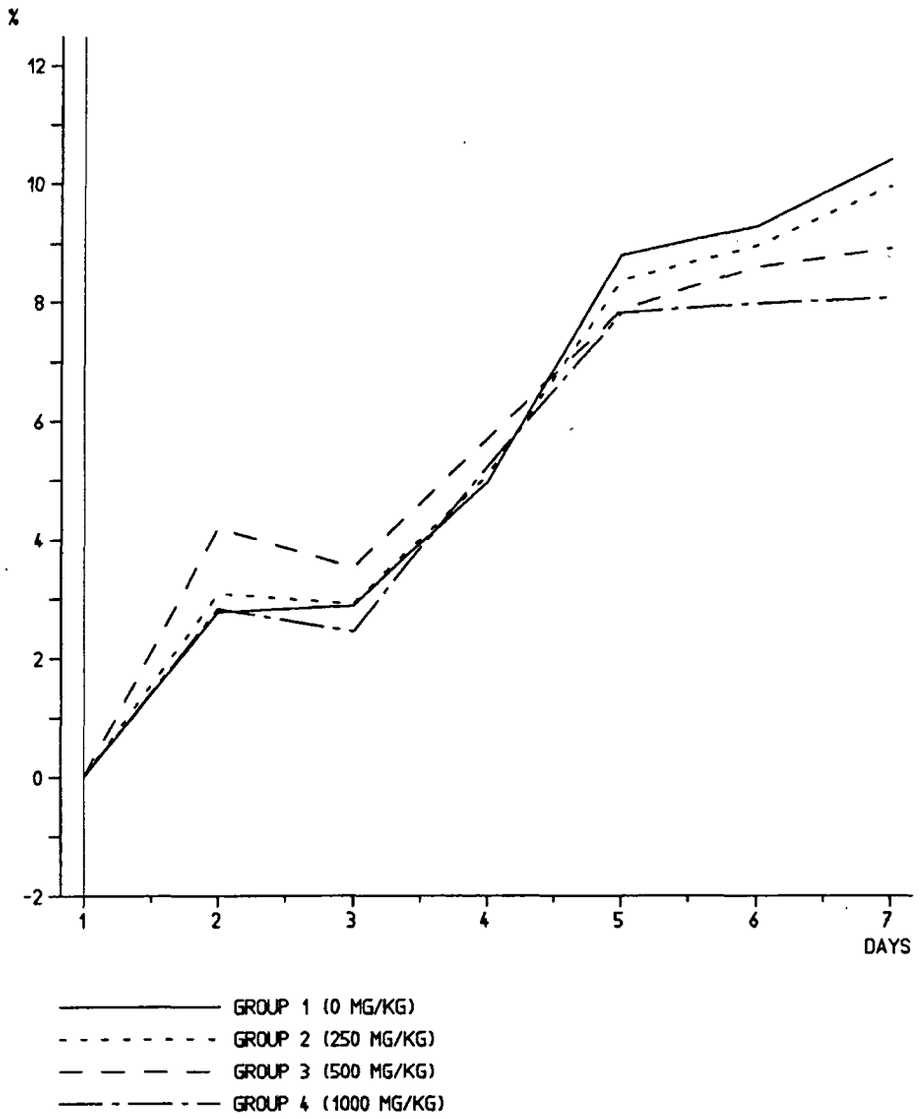
FOOD CONSUMPTION OF MALES
TREATMENT



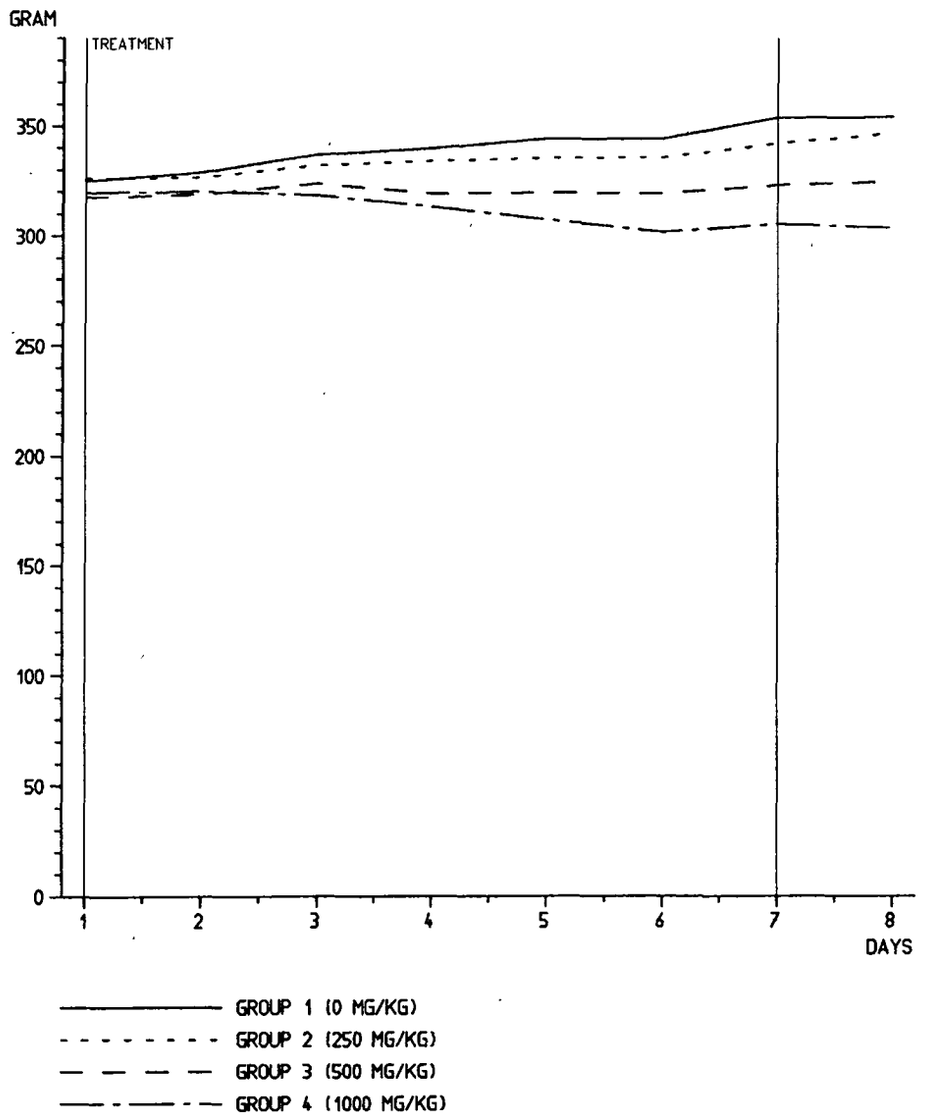
BODY WEIGHTS OF MALES
ACCLIMATIZATION



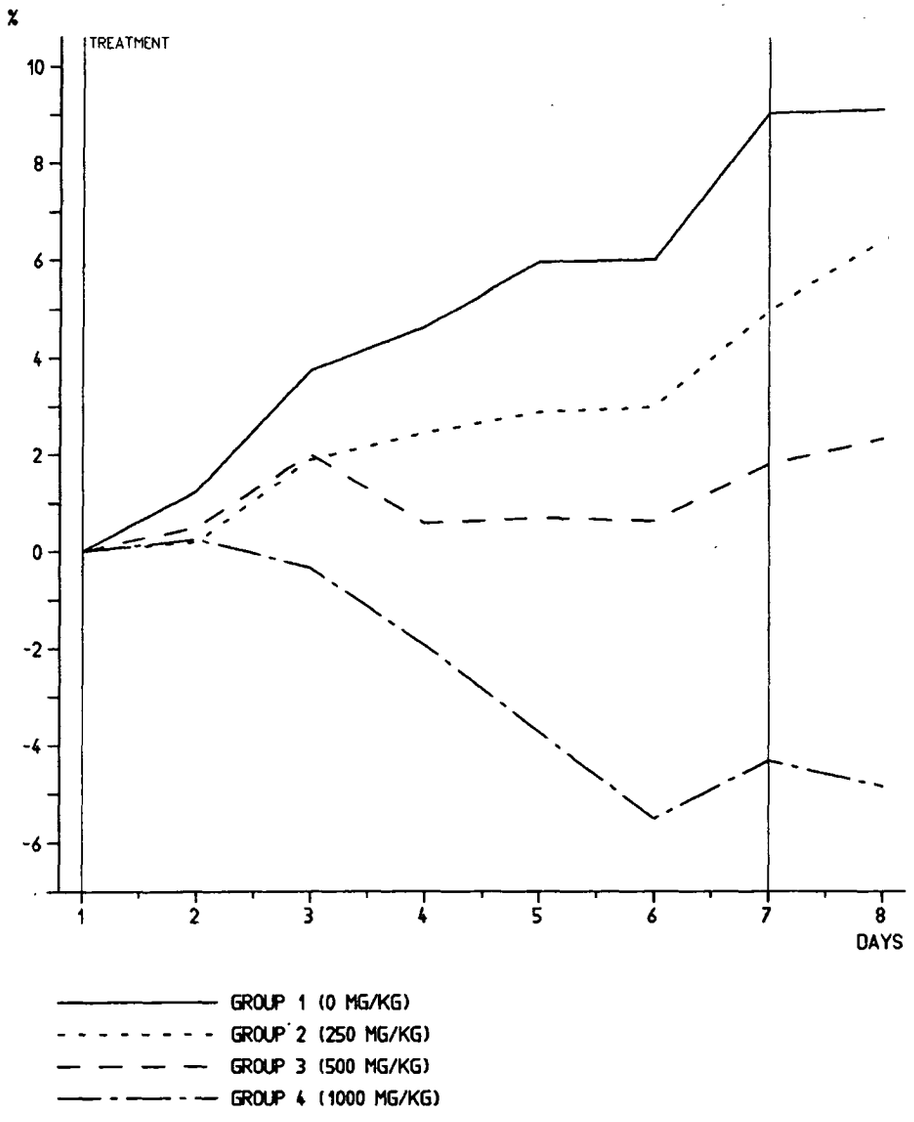
BODY WEIGHT GAIN OF MALES
ACCLIMATIZATION



BODY WEIGHTS OF MALES
TREATMENT



BODY WEIGHT GAIN OF MALES
TREATMENT



BODY WEIGHT GAIN (%) OF FEMALES SUMMARY
TREATMENT

			GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAY	1	MEAN	0	0	0	0
		ST.DEV.	0.0	0.0	0.0	0.0
		N	4	4	4	4
DAY	2	MEAN	1	0	1	1
		ST DEV.	0.4	0.4	0.5	1.3
		N	4	4	4	4
DAY	3	MEAN	3	2	0	0
		ST.DEV.	2.2	2.4	2.8	2.2
		N	4	4	4	4
DAY	4	MEAN	5	3	1 *	-2 **
		ST.DEV.	1.3	1.4	1.3	2 1
		N	4	4	4	4
DAY	5	MEAN	5	3	3	-2 **
		ST.DEV.	0.1	1.9	1.2	2.6
		N	4	4	4	4
DAY	6	MEAN	7	5	4	-2 **
		ST.DEV.	0.4	1.7	1.6	2.4
		N	4	4	4	4
DAY	7	MEAN	8	4	2 *	-2 **
		ST.DEV.	2.4	3.0	3.3	2.3
		N	4	4	4	4
DAY	8	MEAN	9	7	4 *	-1 **
		ST.DEV.	1.8	2.0	2.3	2.2
		N	4	4	4	4

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) OF FEMALES SUMMARY
TREATMENT

			GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAY	1	MEAN	199	203	204	206
		ST.DEV.	6.0	9.2	6.1	5.8
		N	4	4	4	4
DAY	2	MEAN	202	204	206	208
		ST.DEV.	6.3	8.4	5.3	4.5
		N	4	4	4	4
DAY	3	MEAN	206	208	204	206
		ST.DEV.	4.2	13.0	0.4	2.9
		N	4	4	4	4
DAY	4	MEAN	210	209	206	202
		ST.DEV.	5.2	8.5	8.2	4.0
		N	4	4	4	4
DAY	5	MEAN	210	208	209	202
		ST.DEV.	6.4	9.9	4.6	4.9
		N	4	4	4	4
DAY	6	MEAN	213	212	211	202
		ST.DEV.	6.6	8.7	5.3	4.4
		N	4	4	4	4
DAY	7	MEAN	216	212	207	203
		ST.DEV.	3.7	13.1	1.4	5.5
		N	4	4	4	4
DAY	8	MEAN	217	217	212	203
		ST.DEV.	5.7	10.3	10.9	4.9
		N	4	4	4	4

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHT GAIN (%) OF FEMALES SUMMARY
ACCLIMATIZATION

			GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAY	1	MEAN	0	0	0	0
		ST.DEV.	0.0	0.0	0.0	0.0
		N	4	4	4	4
DAY	2	MEAN	4	4	3	4
		ST.DEV.	3.6	0.8	1.2	1.0
		N	4	4	4	4
DAY	3	MEAN	3	5	3	3
		ST.DEV.	3.9	0.6	1.3	2.2
		N	4	4	4	4
DAY	4	MEAN	5	6	8	7
		ST.DEV.	3.8	1.8	2.5	2.7
		N	4	4	4	4
DAY	5	MEAN	10	10	11	10
		ST.DEV.	3.0	1.0	3.5	2.8
		N	4	4	4	4
DAY	6	MEAN	10	10	9	10
		ST.DEV.	2.6	2.1	3.4	2.2
		N	4	4	4	4
DAY	7	MEAN	10	11	10	10
		ST.DEV.	4.1	1.7	4.0	3.5
		N	4	4	4	4

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) OF FEMALES SUMMARY
ACCLIMATIZATION

			GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAY	1	MEAN	181	183	181	184
		ST.DEV.	7.3	9.8	6.8	4.5
		N	4	4	4	4
DAY	2	MEAN	188	190	186	192
		ST.DEV.	5.0	9.9	5.3	3.7
		N	4	4	4	4
DAY	3	MEAN	186	191	187	190
		ST.DEV.	6.0	9.3	6.9	4.5
		N	4	4	4	4
DAY	4	MEAN	190	193	195	196
		ST.DEV.	4.6	8.3	4.0	3.9
		N	4	4	4	4
DAY	5	MEAN	200	201	202	203
		ST.DEV.	5.7	9.6	3.9	5.7
		N	4	4	4	4
DAY	6	MEAN	199	201	197	203
		ST.DEV.	5.3	12.7	1.3	5.0
		N	4	4	4	4
DAY	7	MEAN	199	203	199	202
		ST.DEV.	4.9	11.5	9.4	6.6
		N	4	4	4	4

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

FOOD CONSUMPTION OF FEMALES SUMMARY
(G/ANIMAL/DAY)
TREATMENT

		GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-3	MEAN	16.8	17.1	15.5	13.7 *
	ST.DEV	1.0	1.4	1.3	2.0
	N	4	4	4	4
DAYS 3-5	MEAN	18.9	16.6	16.0	9.5 **
	ST.DEV.	2.1	2.7	1.4	2.9
	N	4	4	4	4
DAYS 5-7	MEAN	17.8	15.3	14.0 **	10.0 **
	ST.DEV.	1.0	1.1	1.9	1.2
	N	4	4	4	4
MEAN OF MEANS		17.9	16.3	15.2	11.1

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

FOOD CONSUMPTION OF FEMALES SUMMARY
(G/ANIMAL/DAY)
ACCLIMATIZATION

		GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-3	MEAN	20.5	20.5	20.2	20.7
	ST.DEV.	2.8	1.4	2.0	2.1
	N	4	4	4	4
DAYS 3-5	MEAN	16.9	18.4	20.2 **	18.4
	ST.DEV.	1.4	0.8	1.4	1.2
	N	4	4	4	4
DAYS 5-7	MEAN	17.8	19.4	17.6	18.5
	ST.DEV.	1.3	2.4	1.2	0.9
	N	4	4	4	4
MEAN OF MEANS		18.4	19.4	19.3	19.2

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHT GAIN (%) OF MALES SUMMARY

TREATMENT

			GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAY	1	MEAN	0	0	0	0
		ST.DEV.	0.0	0.0	0.0	0.0
		N	4	4	4	4
DAY	2	MEAN	1	0	1	0
		ST.DEV.	0.5	1.3	0.7	1.8
		N	4	4	4	4
DAY	3	MEAN	4	2	2	0 *
		ST.DEV.	1.0	1.2	1.0	3.0
		N	4	4	4	4
DAY	4	MEAN	5	2	1	-2 **
		ST.DEV.	0.9	2.2	2.0	3.2
		N	4	4	4	4
DAY	5	MEAN	6	3	1 *	-4 **
		ST.DEV.	1.1	2.2	2.1	2.7
		N	4	4	4	4
DAY	6	MEAN	6	3	1 *	-6 **
		ST.DEV.	1.7	1.9	1.9	2.8
		N	4	4	4	4
DAY	7	MEAN	9	5	2 **	-4 **
		ST.DEV.	1.7	2.7	1.6	3.7
		N	4	4	4	4
DAY	8	MEAN	9	6	2 **	-5 **
		ST.DEV.	1.1	2.7	1.4	4.0
		N	4	4	4	4

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) OF MALES SUMMARY

TREATMENT

			GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAY	1	MEAN	325	326	317	319
		ST.DEV.	9.4	6.8	7.2	4.8
		N	4	4	4	4
DAY	2	MEAN	329	327	319	320
		ST.DEV.	9.6	10.3	9.1	5.9
		N	4	4	4	4
DAY	3	MEAN	337	332	324	318
		ST.DEV.	9.3	9.7	9.7	10.4
		N	4	4	4	4
DAY	4	MEAN	340	334	319	313 *
		ST.DEV.	9.8	13.3	12.6	11.3
		N	4	4	4	4
DAY	5	MEAN	344	335	320 *	308 **
		ST.DEV.	10.7	13.4	12.7	8.3
		N	4	4	4	4
DAY	6	MEAN	344	336	319 *	302 **
		ST.DEV.	12.4	13.0	11.5	7.8
		N	4	4	4	4
DAY	7	MEAN	354	342	323 **	306 **
		ST.DEV.	12.3	15.2	11.3	9.6
		N	4	4	4	4
DAY	8	MEAN	355	347	325 *	304 **
		ST DEV.	13.2	15.6	10.0	9.5
		N	4	4	4	4

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHT GAIN (%) OF MALES SUMMARY
ACCLIMATIZATION

			GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAY	1	MEAN	0	0	0	0
		ST.DEV.	0.0	0.0	0.0	0.0
		N	4	4	4	4
DAY	2	MEAN	3	3	4	3
		ST.DEV.	1.1	0.7	2.2	2.0
		N	4	4	4	4
DAY	3	MEAN	3	3	4	2
		ST.DEV.	1.2	1.1	2.2	1.7
		N	4	4	4	4
DAY	4	MEAN	5	5	6	5
		ST.DEV.	1.4	1.5	2.0	1.1
		N	4	4	4	4
DAY	5	MEAN	9	8	8	8
		ST.DEV.	1.5	2.0	2.6	1.7
		N	4	4	4	4
DAY	6	MEAN	9	9	9	8
		ST.DEV.	2.4	2.2	3.0	2.5
		N	4	4	4	4
DAY	7	MEAN	10	10	9	8
		ST.DEV.	2.3	3.2	2.7	2.3
		N	4	4	4	4

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

BODY WEIGHTS (GRAM) OF MALES SUMMARY
ACCLIMATIZATION

			GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAY	1	MEAN	296	296	294	297
		ST.DEV.	3.4	2.4	3.8	5.6
		N	4	4	4	4
DAY	2	MEAN	304	305	306	305
		ST.DEV.	2.8	3.4	5.1	7.9
		N	4	4	4	4
DAY	3	MEAN	304	305	304	304
		ST.DEV.	3.4	3.4	5.2	6.9
		N	4	4	4	4
DAY	4	MEAN	310	311	311	313
		ST.DEV.	6.4	2.3	5.3	6.0
		N	4	4	4	4
DAY	5	MEAN	322	321	317	320
		ST.DEV.	6.5	4.0	6.3	7.3
		N	4	4	4	4
DAY	6	MEAN	323	323	319	321
		ST.DEV.	9.8	4.6	7.8	6.2
		N	4	4	4	4
DAY	7	MEAN	326	326	320	321
		ST.DEV.	8.6	7.3	8.0	4.2
		N	4	4	4	4

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

FOOD CONSUMPTION OF MALES SUMMARY

(G/ANIMAL/DAY)
TREATMENT

		GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-3	MEAN	24.6	21.2	17.7 *	13.5 **
	ST.DEV.	1.3	2.6	2.9	5.3
	N	4	4	4	4
DAYS 3-5	MEAN	26.7	21.6 *	16.6 **	9.2 **
	ST.DEV.	2.0	1.5	3.5	2.4
	N	4	4	4	4
DAYS 5-7	MEAN	25.5	21.1 *	17.1 **	11.6 **
	ST.DEV.	1.6	2.4	1.2	3.2
	N	4	4	4	4
MEAN OF MEANS		25.6	21.3	17.1	11.5

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

FOOD CONSUMPTION OF MALES SUMMARY
(G/ANIMAL/DAY)
ACCLIMATIZATION

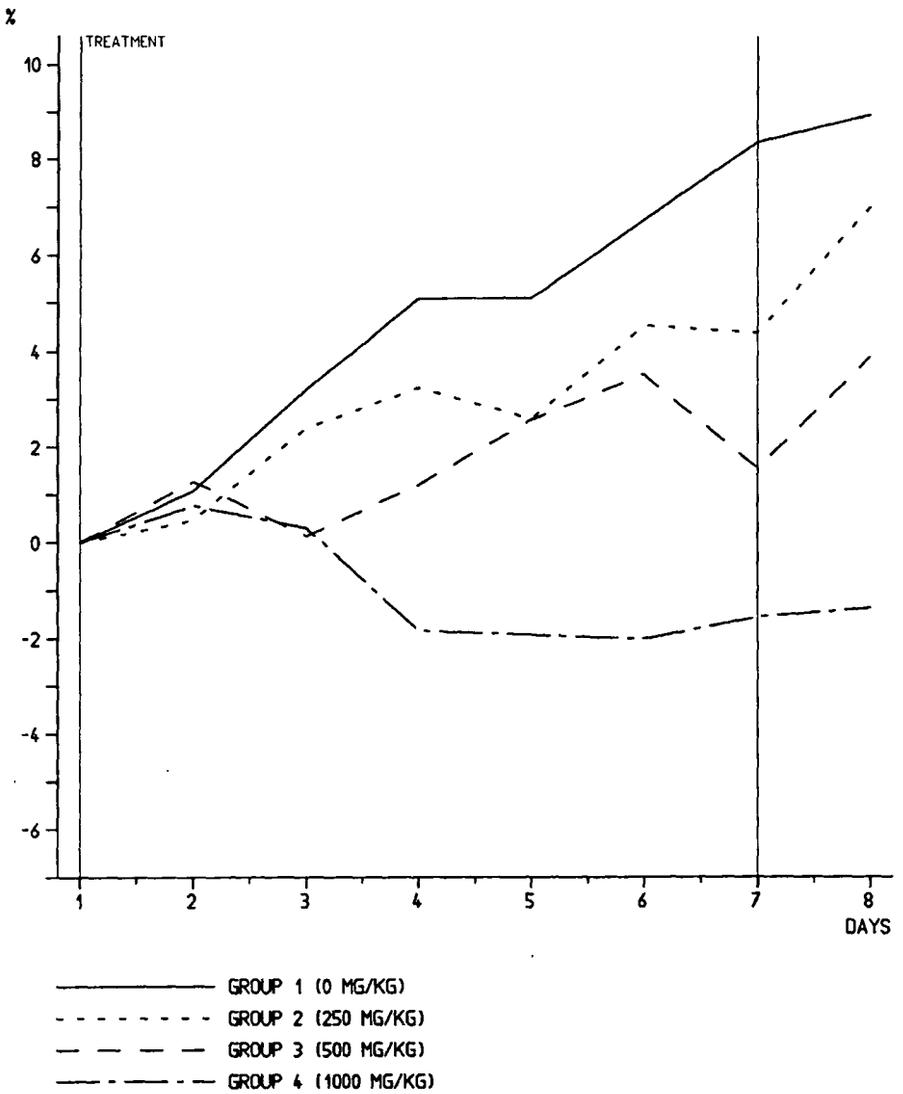
		GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
DAYS 1-3	MEAN	25.6	22.9	21.7 *	24.6
	ST.DEV	2.0	1.5	1.3	1.5
	N	4	4	4	4
DAYS 3-5	MEAN	25.6	24.2	24.3	24.8
	ST.DEV.	2.5	1.8	3.7	1.3
	N	4	4	4	4
DAYS 5-7	MEAN	25.5	24.5	22.2	24.6
	ST.DEV.	2.1	1.9	4.5	2.9
	N	4	4	4	4
MEAN OF MEANS		25.6	23.9	22.7	24.7

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

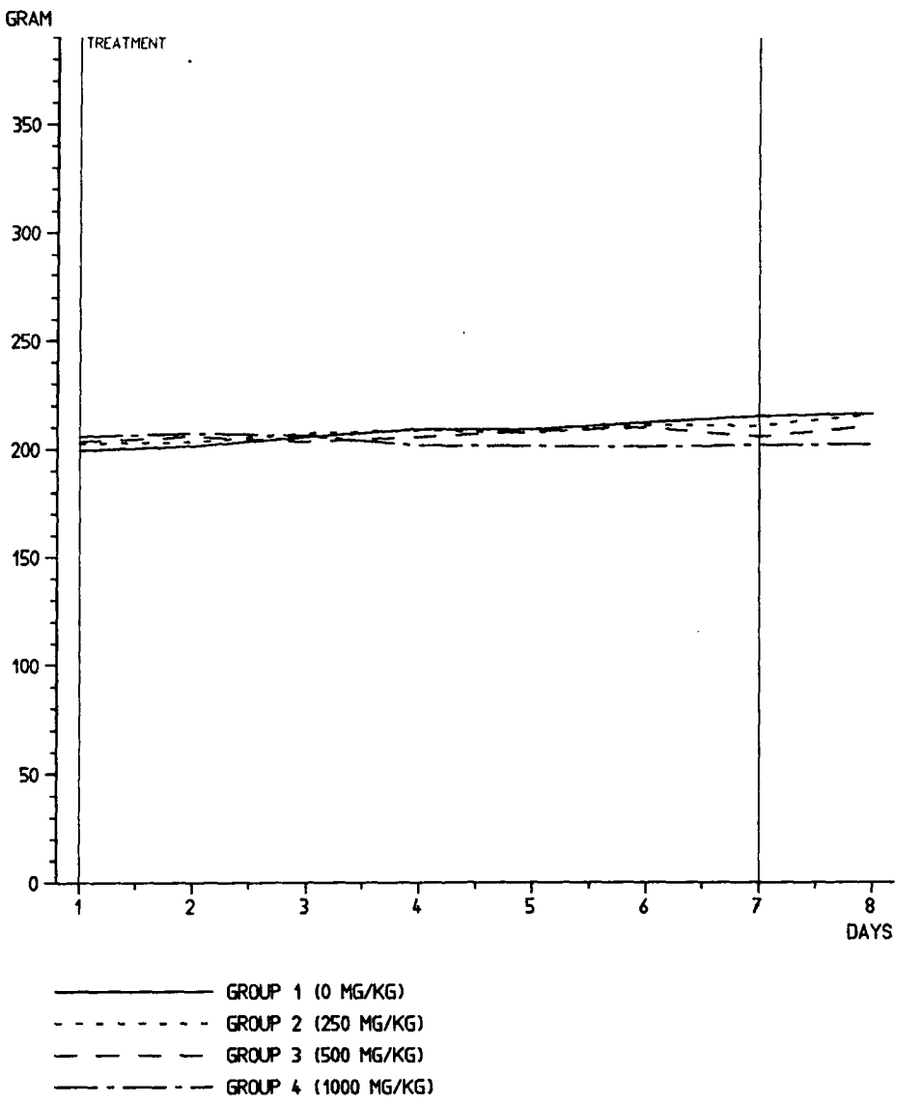
8.1 IN LIFE DATA

8 SUMMARY DATA

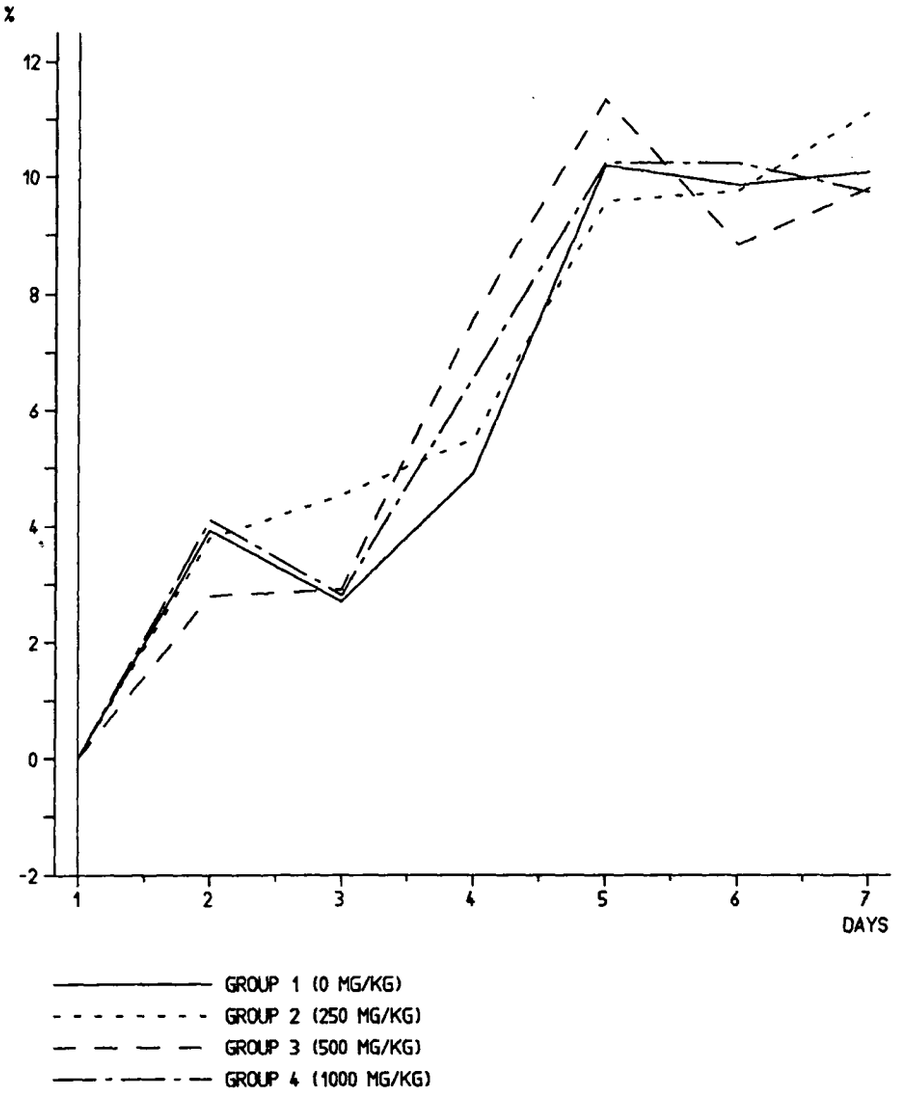
BODY WEIGHT GAIN OF FEMALES
TREATMENT



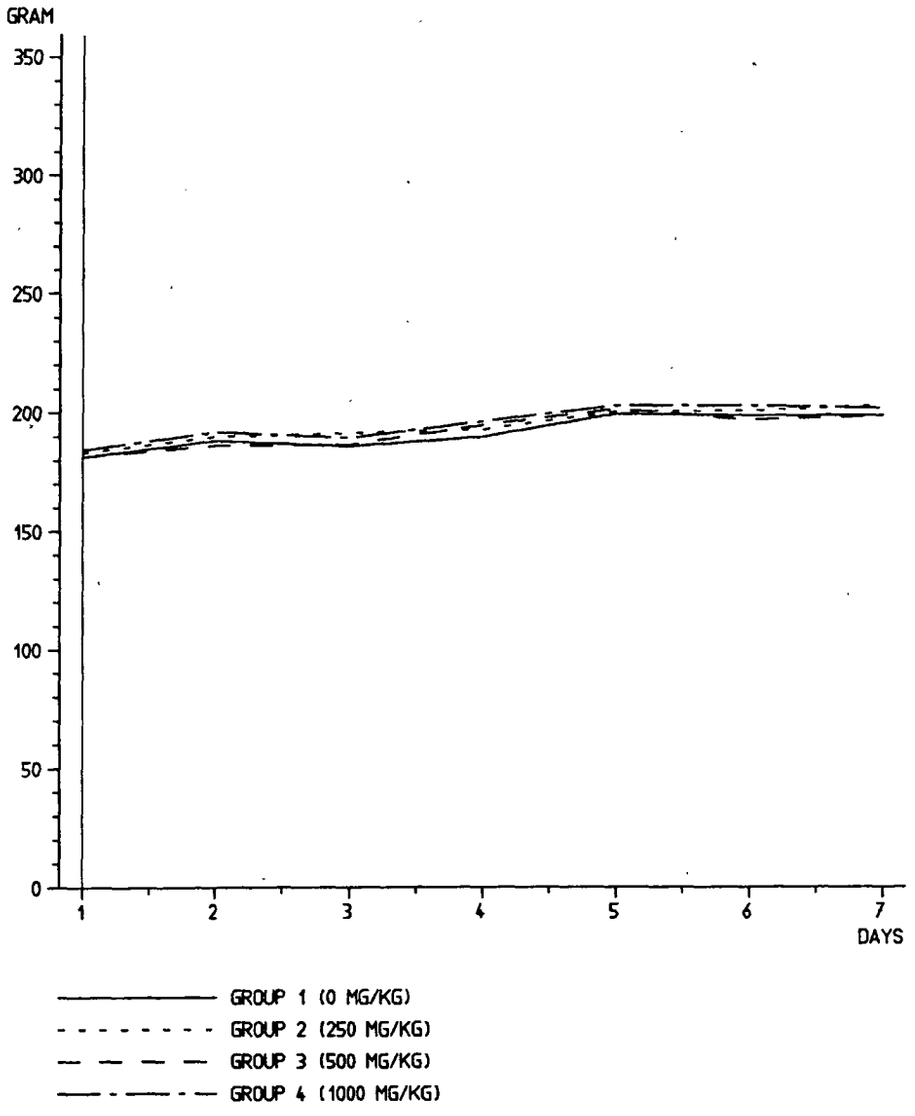
BODY WEIGHTS OF FEMALES
TREATMENT



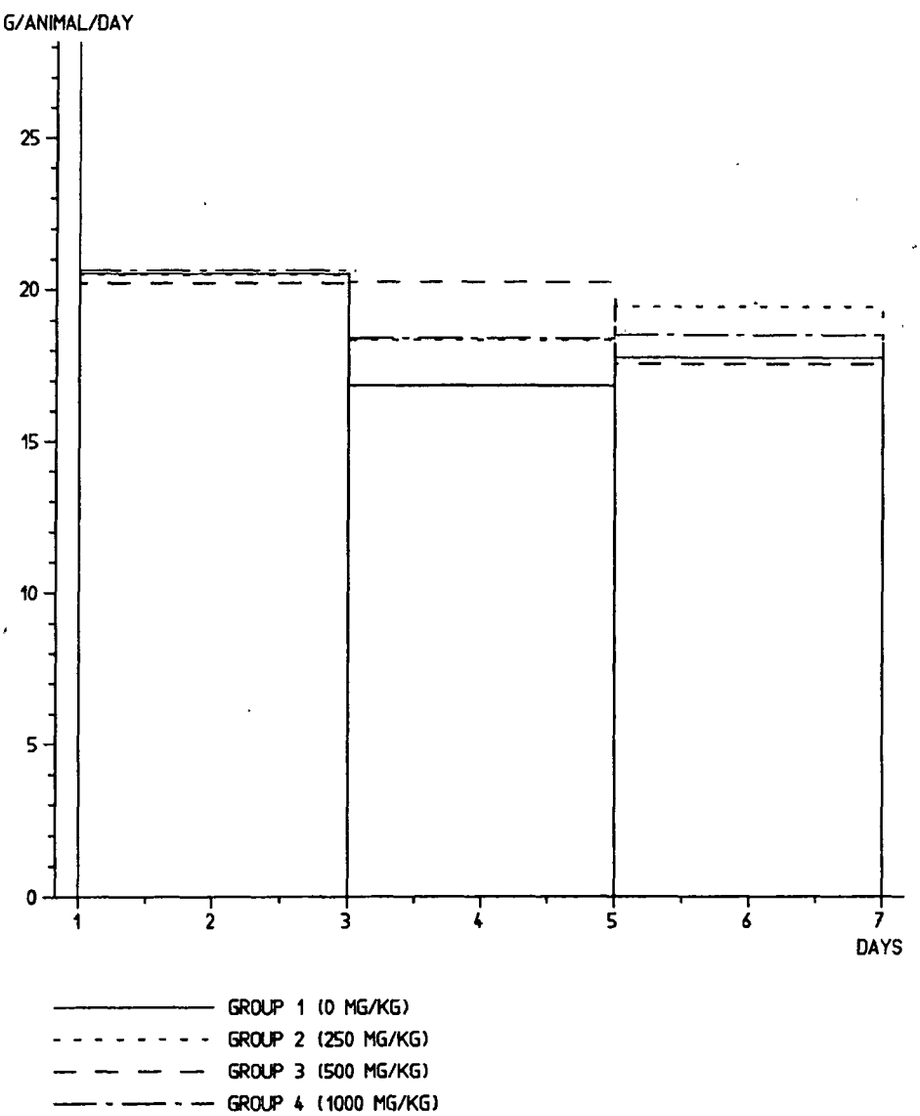
BODY WEIGHT GAIN OF FEMALES
ACCLIMATIZATION



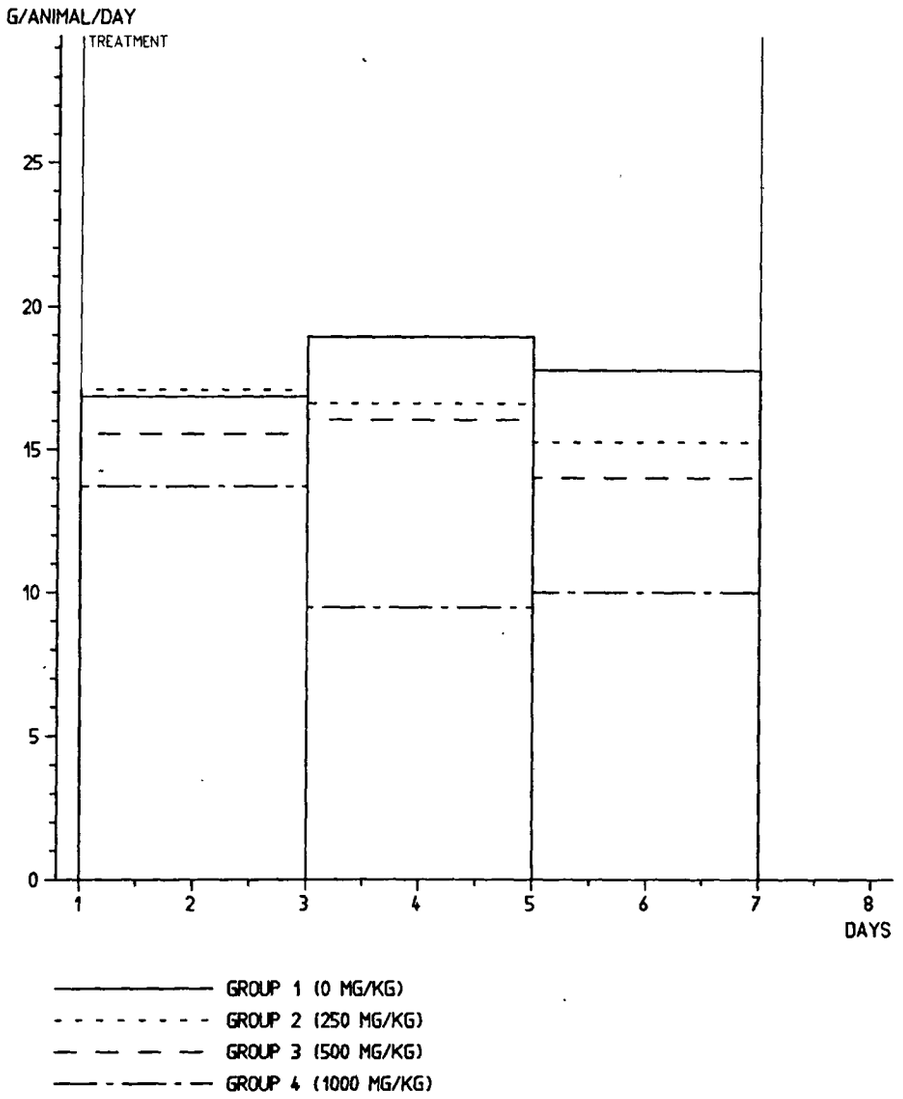
BODY WEIGHTS OF FEMALES
ACCLIMATIZATION



FOOD CONSUMPTION OF FEMALES
ACCLIMATIZATION



FOOD CONSUMPTION OF FEMALES
TREATMENT



DAILY CLINICAL SIGNS AND OBSERVATIONS - MALES

ACCLIMATIZATION PERIOD

Group 1 (0 mg/kg)

Male	Noted on days						
No.	1	2	3	4	5	6	7
1	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-

Group 2 (250 mg/kg)

Male	Noted on days						
No.	1	2	3	4	5	6	7
5	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-

Group 3 (500 mg/kg)

Male	Noted on days						
No.	1	2	3	4	5	6	7
9	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-
11	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-

Group 4 (1000 mg/kg)

Male	Noted on days						
No.	1	2	3	4	5	6	7
13	-	-	-	-	-	-	-
14	-	-	-	-	-	-	-
15	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-

- No clinical signs or observations were noted

DAILY CLINICAL SIGNS AND OBSERVATIONS - MALES

TREATMENT PERIOD

Group 1 (0 mg/kg)

Male No.	Noted on days 1	2	3	4	5	6	7	8
1	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-

Group 2 (250 mg/kg)

Male No.	Noted on days 1	2	3	4	5	6	7	8
5	-	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-	-

Group 3 (500 mg/kg)

Male No.	Noted on days 1	2	3	4	5	6	7	8
9	A	-	-	A C	A C	A B C	A B C	C
10	-	-	C D	A C D	A C	C	C	C
11	-	-	-	C	A C	C	C	C
12	-	-	C	C	A C	C	C	C

Group 4 (1000 mg/kg)

Male No.	Noted on days 1	2	3	4	5	6	7	8
13	A B	A B	A B C D E	A B C D	A B C	A B C F	A B C E F	C E F
14	A	A B C	A B C D E	A B C D	A B C	A B C D E F	A B C E F	C E F
15	A	A B	A B C D E	A B C D	A B C	A B C D E F	A B C E F	C E F
16	A B C	A B C	A B C D E	A B C D	A B C	A B C F	A B C E F	C E F

- No clinical signs or observations were noted

A = Sedation
B = Ventral recumbency
C = Ruffled fur
D = Uncoordinated movements
E = Hunched posture
F = Paws, bluish appearance

DAILY CLINICAL SIGNS AND OBSERVATIONS - FEMALES

ACCLIMATIZATION PERIOD

Group 1 (0 mg/kg)

Female No.	Noted on days 1	2	3	4	5	6	7
17	-	-	-	-	-	-	-
18	-	-	-	-	-	-	-
19	-	-	-	-	-	-	-
20	-	-	-	-	-	-	-

Group 2 (250 mg/kg)

Female No.	Noted on days 1	2	3	4	5	6	7
21	-	-	-	-	-	-	-
22	-	-	-	-	-	-	-
23	-	-	-	-	-	-	-
24	-	-	-	-	-	-	-

Group 3 (500 mg/kg)

Female No.	Noted on days 1	2	3	4	5	6	7
25	-	-	-	-	-	-	-
26	-	-	-	-	-	-	-
27	-	-	-	-	-	-	-
28	-	-	-	-	-	-	-

Group 4 (1000 mg/kg)

Female No.	Noted on days 1	2	3	4	5	6	7
29	-	-	-	-	-	-	-
30	-	-	-	-	-	-	-
31	-	-	-	-	-	-	-
32	-	-	-	-	-	-	-

- No clinical signs or observations were noted

DAILY CLINICAL SIGNS AND OBSERVATIONS - FEMALES

TREATMENT PERIOD

Group 1 (0 mg/kg)

Female No.	Noted on days 1	2	3	4	5	6	7	8
17	-	-	-	-	-	-	-	-
18	-	-	-	-	-	-	-	-
19	-	-	-	-	-	-	-	-
20	-	-	-	-	-	-	-	-

Group 2 (250 mg/kg)

Female No.	Noted on days 1	2	3	4	5	6	7	8
21	-	-	-	-	-	-	-	-
22	-	-	-	-	-	-	-	-
23	-	-	-	-	-	-	-	-
24	-	-	-	-	-	-	-	-

Group 3 (500 mg/kg)

Female No.	Noted on days 1	2	3	4	5	6	7	8
25	-	-	-	-	-	-	-	-
26	-	-	-	-	-	-	-	-
27	-	-	-	-	-	-	-	-
28	A	-	-	-	-	-	-	-

Group 4 (1000 mg/kg)

Female No.	Noted on days 1	2	3	4	5	6	7	8
29	A B	A B	-	-	-	A C F	C F	C
30	A B D	A B	A B C D	C D	A C	A C F	A B C F	C
31	A B	A B	-	C D	D	A C F	C F	C
32	A B	A B	A B C D	C D	A C	A C F	C F	C

- No clinical signs or observations were noted

A = Sedation
B = Ventral recumbency
C = Ruffled fur
D = Uncoordinated movements
E = Hunched posture
F = Paws, bluish appearance

8.2 NECROPSY DATA

MACROSCOPICAL FINDINGS SUMMARY

ALL NECROPSIES
MALES

	GROUP 1 0 MG/KG		GROUP 2 250 MG/KG		GROUP 3 500 MG/KG		GROUP 4 1000 MG/KG	
ANIMALS EXAMINED	4		4		4		4	
ANIMALS WITHOUT FINDINGS	3		0		0		0	
ANIMALS AFFECTED:								
LIVER.....								
REDUCED IN SIZE	0	0%	1	25%	0	0%	0	0%
KIDNEYS.....								
PELVIC DILATION	1	25%	0	0%	0	0%	0	0%
SPLEEN.....								
ENLARGED	0	0%	4 #	100%	4 #	100%	4 #	100%
LYMPH NODES.....								
DISCOLORATION	0	0%	0	0%	0	0%	3	75%
ENLARGED	0	0%	0	0%	0	0%	2	50%

/ ## : Fisher's Exact Test based on counts significant at 5% (#) or 1% (##) level

MACROSCOPICAL FINDINGS SUMMARY

ALL NECROPSIES
FEMALES

	GROUP 1 0 MG/KG		GROUP 2 250 MG/KG		GROUP 3 500 MG/KG		GROUP 4 1000 MG/KG	
ANIMALS EXAMINED	4		4		4		4	
ANIMALS WITHOUT FINDINGS	3		0		0		0	
ANIMALS AFFECTED:								
KIDNEYS.....								
PELVIC DILATION	1	25%	1	25%	0	0%	0	0%
SPLEEN.....								
ENLARGED	0	0%	4 #	100%	4 #	100%	4 #	100%

/ ## : Fisher's Exact Test based on counts significant at 5% (#) or 1% (##) level

ORGAN WEIGHTS (GRAM) SUMMARY
MALES

		GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
BODY W.	MEAN	349.3	340.5	319.1 **	298.6 **
	ST.DEV.	9.8	14.8	10.5	9.7
	N	4	4	4	4
LIVER	MEAN	15.71	13.58	13.98	13.62
	ST.DEV.	1.45	1.61	1.22	1.58
	N	4	4	4	4
KIDNEYS	MEAN	2.69	2.47	2.47	2.64
	ST.DEV.	0.31	0.18	0.30	0.30
	N	4	4	4	4
SPLEEN	MEAN	0.71	2.62 **	3.14 **	2.92 **
	ST.DEV.	0.03	0.51	0.46	0.48
	N	4	4	4	4
TESTES	MEAN	3.45	3.73	3.45	3.48
	ST.DEV.	0.20	0.29	0.23	0.21
	N	4	4	4	4
PROSTATE	MEAN	0.77	0.67	0.68	0.57
	ST.DEV.	0.14	0.18	0.10	0.10
	N	4	4	4	4
EPIDIDYMIDES	MEAN	1.069	1.127	1.150	1.132
	ST.DEV.	0.139	0.152	0.082	0.121
	N	4	4	4	4
SEMINAL VE	MEAN	1.07	1.28	1.33	1.09
	ST.DEV.	0.43	0.44	0.14	0.36
	N	4	4	4	4

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN/BODY WEIGHT RATIOS SUMMARY

MALES

		GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
BODY W.	MEAN	349.3	340.5	319.1 **	298.6 **
(GRAM)	ST.DEV.	9.8	14.8	10.5	9.7
	N	4	4	4	4
LIVER	MEAN	4.50	3.98	4.37	4.55
(%)	ST.DEV.	0.41	0.34	0.24	0.38
	N	4	4	4	4
KIDNEYS	MEAN	0.77	0.73	0.77	0.88
(%)	ST.DEV.	0.07	0.03	0.08	0.08
	N	4	4	4	4
SPLEEN	MEAN	0.20	0.77 **	0.98 **	0.97 **
(%)	ST.DEV.	0.01	0.13	0.12	0.13
	N	4	4	4	4
TESTES	MEAN	0.99	1.09	1.08	1.17 **
(%)	ST.DEV.	0.06	0.06	0.06	0.06
	N	4	4	4	4
PROSTATE	MEAN	0.22	0.19	0.21	0.19
(%)	ST.DEV.	0.04	0.05	0.02	0.03
	N	4	4	4	4
EPIDIDYMIDES	MEAN	0.306	0.332	0.361	0.379
(%)	ST.DEV.	0.040	0.054	0.033	0.042
	N	4	4	4	4
SEMINAL VE	MEAN	0 31	0.38	0.42	0.36
(%)	ST.DEV.	0.12	0.15	0.06	0.12
	N	4	4	4	4

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN WEIGHTS (GRAM) SUMMARY
FEMALES

		GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
BODY W.	MEAN	212.0	211.6	208.3	198.1
	ST.DEV.	5.3	9.0	10.5	4.3
	N	4	4	4	4
LIVER	MEAN	8.80	9.05	10.09 *	9.87
	ST.DEV.	0.48	0.59	0.65	0.67
	N	4	4	4	4
KIDNEYS	MEAN	1.76	1.77	1.81	1 67
	ST.DEV.	0.15	0.08	0.09	0.07
	N	4	4	4	4
SPLEEN	MEAN	0.55	2.22 **	2.77 **	2.52 **
	ST.DEV.	0.06	0.41	0.33	0.34
	N	4	4	4	4
OVARIES	MEAN	0.124	0.101	0.118	0.114
	ST.DEV.	0.007	0.018	0.011	0.011
	N	4	4	4	4
UTERUS	MEAN	0.91	0.98	0.74	1.00
	ST.DEV.	0.39	0.36	0.10	0.40
	N	4	4	4	4

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

ORGAN/BODY WEIGHT RATIOS SUMMARY

FEMALES

		GROUP 1 0 MG/KG	GROUP 2 250 MG/KG	GROUP 3 500 MG/KG	GROUP 4 1000 MG/KG
BODY W. (GRAM)	MEAN	212.0	211.6	208.3	198.1
	ST.DEV.	5.3	9.0	10.5	4.3
	N	4	4	4	4
LIVER (%)	MEAN	4.16	4.28	4.85 **	4.98 **
	ST.DEV.	0.30	0.18	0.21	0.32
	N	4	4	4	4
KIDNEYS (%)	MEAN	0 83	0.84	0.87	0.84
	ST.DEV.	0.08	0.02	0.04	0.04
	N	4	4	4	4
SPLEEN (%)	MEAN	0.26	1.05 **	1.33 **	1.27 **
	ST.DEV.	0.03	0.18	0.10	0.16
	N	4	4	4	4
OVARIES (%)	MEAN	0.059	0.048	0.057	0.058
	ST.DEV.	0.004	0.007	0.008	0.006
	N	4	4	4	4
UTERUS (%)	MEAN	0.43	0.46	0.36	0.50
	ST.DEV.	0.19	0.15	0.06	0.20
	N	4	4	4	4

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

9 INDIVIDUAL DATA

9.1 IN LIFE DATA

FOOD CONSUMPTION (G/ANIMAL/DAY) OF MALES

ACCLIMATIZATION

GROUP 1 (0 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
1	26.3	27.3	27.0
2	24.5	22.3	23.1
3	23.6	25.2	24.3
4	28.0	27.7	27.6

FOOD CONSUMPTION (G/ANIMAL/DAY) OF MALES

ACCLIMATIZATION

GROUP 2 (250 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
5	25.1	25.0	26.3
6	22.1	26.2	25.8
7	22.5	23.5	23.7
8	22.0	22.1	22.2

FOOD CONSUMPTION (G/ANIMAL/DAY) OF MALES

ACCLIMATIZATION

GROUP 3 (500 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
9	23.6	25.7	26.5
10	20.4	20.3	21.0
11	21.4	22.3	24.8
12	21.6	28.8	16.4

FOOD CONSUMPTION (G/ANIMAL/DAY) OF MALES

ACCLIMATIZATION

GROUP 4 (1000 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
13	22.8	25.5	28.4
14	26.4	23.1	21.7
15	24.3	24.8	24.6
16	25.0	26.0	23.6

FOOD CONSUMPTION (G/ANIMAL/DAY) OF MALES

TREATMENT

GROUP 1 (0 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
1	23.5	25.6	23.6
2	24.4	25.3	25.5
3	24.0	26.3	25.3
4	26.5	29.7	27.6

FOOD CONSUMPTION (G/ANIMAL/DAY) OF MALES

TREATMENT

GROUP 2 (250 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
5	23.6	22.3	23.3
6	23.1	22.6	23.0
7	20.2	22.0	19.7
8	17.9	19.3	18.5

FOOD CONSUMPTION (G/ANIMAL/DAY) OF MALES

TREATMENT

GROUP 3 (500 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
9	20.7	20.4	18.2
10	14.2	12.5	16.4
11	16.5	18.5	17.9
12	19.3	15.2	15.7

FOOD CONSUMPTION (G/ANIMAL/DAY) OF MALES

TREATMENT

GROUP 4 (1000 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
13	18.1	9.3	7.8
14	9.9	9.1	13.6
15	18.1	12.2	14.8
16	8.1	6.4	10.3

BODY WEIGHTS (GRAM) OF MALES
ACCLIMATIZATION

GROUP 1 (0 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7
1	299	303	302	311	322	324	325
2	291	301	300	301	312	309	315
3	296	308	306	316	326	330	335
4	297	303	308	312	326	329	331

BODY WEIGHTS (GRAM) OF MALES
ACCLIMATIZATION

GROUP 2 (250 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7
5	297	304	304	309	321	322	323
6	293	301	302	313	322	324	331
7	296	308	310	314	325	328	332
8	299	308	304	309	316	317	317

BODY WEIGHTS (GRAM) OF MALES

ACCLIMATIZATION

GROUP 3 (500 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7
9	292	303	300	310	318	322	325
10	294	301	300	303	308	308	309
11	299	309	307	315	320	323	326
12	290	312	310	314	322	323	321

BODY WEIGHTS (GRAM) OF MALES
ACCLIMATIZATION

GROUP 4 (1000 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7
13	289	299	298	306	314	319	320
14	300	311	310	314	321	315	316
15	299	298	298	311	316	319	322
16	301	314	311	320	330	330	326

BODY WEIGHT GAIN (%) OF MALES
ACCLIMATIZATION

GROUP 1 (0 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7
1	0	1	1	4	8	8	9
2	0	3	3	4	7	6	8
3	0	4	3	7	10	12	13
4	0	2	4	5	10	11	11

BODY WEIGHT GAIN (%) OF MALES
ACCLIMATIZATION

GROUP 2 (250 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7
5	0	2	2	4	8	8	9
6	0	3	3	7	10	11	13
7	0	4	4	6	10	11	12
8	0	3	2	3	6	6	6

BODY WEIGHT GAIN (%) OF MALES

ACCLIMATIZATION

GROUP 3 (500 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7
9	0	4	3	6	9	10	11
10	0	2	2	3	5	5	5
11	0	3	3	5	7	8	9
12	0	7	7	8	11	11	10

BODY WEIGHT GAIN (%) OF MALES
ACCLIMATIZATION

GROUP 4 (1000 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7
13	0	3	3	6	9	10	11
14	0	4	3	5	7	5	5
15	0	0	0	4	6	7	8
16	0	4	3	6	10	10	8

BODY WEIGHTS (GRAM) OF MALES

TREATMENT

GROUP 1 (0 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7	8
1	320	322	329	332	334	332	342	345
2	314	320	330	332	336	337	347	342
3	335	340	348	351	356	359	369	369
4	329	333	341	345	351	350	360	362

BODY WEIGHTS (GRAM) OF MALES

TREATMENT

GROUP 2 (250 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7	8
5	324	326	331	334	329	330	342	346
6	330	334	341	345	349	347	354	359
7	333	334	338	342	344	346	352	358
8	317	312	319	315	320	320	321	325

BODY WEIGHTS (GRAM) OF MALES

TREATMENT

GROUP 3 (500 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7	8
9	319	320	329	327	329	328	330	333
10	307	306	310	302	302	304	307	310
11	323	328	331	329	329	329	332	330
12	320	321	325	319	319	317	323	326

) OF MALES

3	4	5	6	7	8
325	321	310	300	301	298
309	304	302	299	307	308
330	325	318	313	319	315
310	304	300	295	296	294

BODY WEIGHT GAIN (%) OF MALES

TREATMENT

GROUP 1 (0 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7	8
1	0	1	3	4	4	4	7	8
2	0	2	5	6	7	7	10	9
3	0	1	4	5	6	7	10	10
4	0	1	4	5	7	6	9	10

BODY WEIGHT GAIN (%) OF MALES

TREATMENT

GROUP 2 (250 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7	8
5	0	1	2	3	1	2	5	7
6	0	1	3	4	6	5	7	9
7	0	0	2	3	4	4	6	8
8	0	-2	1	-1	1	1	1	3

BODY WEIGHT GAIN (%) OF MALES

TREATMENT

GROUP 3 (500 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7	8
9	0	0	3	3	3	3	4	4
10	0	0	1	-2	-2	-1	0	1
11	0	1	2	2	2	2	3	2
12	0	0	2	0	0	-1	1	2

BODY WEIGHT GAIN (%) OF MALES

TREATMENT

GROUP 4 (1000 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7	8
13	0	0	0	-1	-4	-7	-7	-8
14	0	1	-1	-3	-3	-4	-2	-1
15	0	2	3	2	-1	-2	0	-1
16	0	-2	-4	-6	-7	-8	-8	-9

FOOD CONSUMPTION (G/ANIMAL/DAY) OF FEMALES

ACCLIMATIZATION

GROUP 1 (0 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
17	17.9	18.5	17.6
18	18.6	17.4	16.7
19	23.8	15.3	17.2
20	21.9	16.2	19.7

FOOD CONSUMPTION (G/ANIMAL/DAY) OF FEMALES

ACCLIMATIZATION

GROUP 2 (250 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
21	22.3	19.0	21.5
22	20.0	19.0	19.3
23	18.9	17.9	16.1
24	20.8	17.5	20.8

FOOD CONSUMPTION (G/ANIMAL/DAY) OF FEMALES

ACCLIMATIZATION

GROUP 3 (500 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
25	17.9	18.3	16.3
26	20.2	20.4	17.6
27	22.9	21.8	19.1
28	19.7	20.4	17.3

FOOD CONSUMPTION (G/ANIMAL/DAY) OF FEMALES

ACCLIMATIZATION

GROUP 4 (1000 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
29	18.1	17.2	18.7
30	21.3	18.4	17.6
31	23.2	20.1	19.8
32	20.0	18.0	18.1

FOOD CONSUMPTION (G/ANIMAL/DAY) OF FEMALES

TREATMENT

GROUP 1 (0 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
17	17.7	21.7	18.7
18	16.5	16.7	17.6
19	15.6	18.6	16.4
20	17.6	18.7	18.4

FOOD CONSUMPTION (G/ANIMAL/DAY) OF FEMALES

TREATMENT

GROUP 2 (250 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
21	18.0	15.8	16.0
22	17.2	18.6	15.9
23	15.0	13.2	13.7
24	18.1	18.9	15.4

FOOD CONSUMPTION (G/ANIMAL/DAY) OF FEMALES

TREATMENT

GROUP 3 (500 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
25	14.2	15.2	11.6
26	15.1	15.4	13.5
27	15.5	18.2	15.1
28	17.4	15.4	15.8

FOOD CONSUMPTION (G/ANIMAL/DAY) OF FEMALES

TREATMENT

GROUP 4 (1000 MG/KG)

DAYS ANIMAL	1-3	3-5	5-7
29	11.6	9.5	8.8
30	12.5	6.1	10.1
31	15.2	13.2	11.6
32	15.6	9.2	9.4

BODY WEIGHTS (GRAM) OF FEMALES

ACCLIMATIZATION

GROUP 1 (0 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7
17	178	183	188	195	203	196	200
18	190	190	185	191	202	202	198
19	173	186	179	184	191	193	194
20	183	194	193	191	203	205	206

BODY WEIGHTS (GRAM) OF FEMALES

ACCLIMATIZATION

GROUP 2 (250 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7
21	197	204	205	205	215	219	220
22	175	181	184	188	194	194	198
23	179	185	186	190	196	190	194
24	181	190	190	188	197	201	202

BODY WEIGHTS (GRAM) OF FEMALES
ACCLIMATIZATION

GROUP 3 (500 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7
25	190	194	194	198	202	199	202
26	180	184	186	195	201	196	200
27	181	187	189	198	206	198	208
28	174	181	177	189	197	196	186

BODY WEIGHTS (GRAM) OF FEMALES

ACCLIMATIZATION

GROUP 4 (1000 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7
29	178	187	184	193	198	199	197
30	184	193	194	201	209	205	209
31	189	195	193	198	207	210	206
32	186	192	187	193	199	199	197

BODY WEIGHT GAIN (%) OF FEMALES

ACCLIMATIZATION

GROUP 1 (0 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7
17	0	2	5	9	14	10	12
18	0	0	-3	0	6	6	4
19	0	8	3	6	10	12	12
20	0	6	5	4	11	12	12

BODY WEIGHT GAIN (%) OF FEMALES

ACCLIMATIZATION

GROUP 2 (250 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7
21	0	3	4	4	9	11	12
22	0	4	5	8	11	11	13
23	0	3	4	6	10	7	9
24	0	5	5	4	9	11	11

BODY WEIGHT GAIN (%) OF FEMALES

ACCLIMATIZATION

GROUP 3 (500 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7
25	0	2	2	4	6	5	6
26	0	2	3	8	12	9	11
27	0	3	5	9	14	9	15
28	0	4	2	9	14	13	7

BODY WEIGHT GAIN (%) OF FEMALES

ACCLIMATIZATION

GROUP 4 (1000 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7
29	0	5	3	8	11	12	10
30	0	5	6	10	14	12	14
31	0	3	2	5	10	11	9
32	0	3	0	4	7	7	6

BODY WEIGHTS (GRAM) OF FEMALES

TREATMENT

GROUP 1 (0 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7	8
17	205	207	205	214	216	220	215	225
18	200	203	208	207	211	213	219	214
19	191	193	200	203	201	204	211	212
20	202	203	210	214	212	215	219	218

BODY WEIGHTS (GRAM) OF FEMALES

TREATMENT

GROUP 2 (250 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7	8
21	216	216	226	221	221	224	229	231
22	198	199	200	203	206	206	207	214
23	197	198	197	203	198	204	198	206
24	199	201	208	209	206	213	213	217

BODY WEIGHTS (GRAM) OF FEMALES

TREATMENT

GROUP 3 (500 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7	8
25	203	206	203	208	209	211	205	212
26	205	207	204	206	208	208	205	213
27	210	213	204	215	215	218	208	224
28	196	200	203	195	204	206	208	197

BODY WEIGHTS (GRAM) OF FEMALES

TREATMENT

GROUP 4 (1000 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7	8
29	203	204	205	201	203	201	201	200
30	212	210	206	202	200	200	202	203
31	209	212	211	208	208	208	211	210
32	199	204	204	198	197	198	198	200

BODY WEIGHT GAIN (%) OF FEMALES

TREATMENT

GROUP 1 (0 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7	8
17	0	1	0	4	5	7	5	10
18	0	2	4	4	5	6	10	7
19	0	1	5	6	5	7	11	11
20	0	1	4	6	5	6	8	8

BODY WEIGHT GAIN (%) OF FEMALES

TREATMENT

GROUP 2 (250 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7	8
21	0	0	4	2	2	3	6	7
22	0	1	1	3	4	4	5	8
23	0	0	0	3	0	4	0	4
24	0	1	4	5	4	7	7	9

BODY WEIGHT GAIN (%) OF FEMALES

TREATMENT

GROUP 3 (500 MG/KG)

DAYS ANIMAL	1	2	3	4	5	6	7	8
25	0	1	0	2	3	4	1	4
26	0	1	-1	0	1	1	0	4
27	0	1	-3	2	2	4	-1	6
28	0	2	4	0	4	5	6	1

BODY WEIGHT GAIN (%) OF FEMALES

TREATMENT

GROUP 4 (1000 MG/KG)

DAYS / ANIMAL	1	2	3	4	5	6	7	8
29	0	0	1	-1	0	-1	-1	-1
30	0	-1	-3	-5	-6	-6	-5	-4
31	0	1	1	-1	-1	-1	1	0
32	0	2	2	-1	-1	-1	-1	0

9.2 NECROPSY DATA

MORTALITY DATA

MALES

GROUP 1 (0 MG/KG)

ANIMAL	SCHEDULED NECROPSY	DAY OF DEATH
1	07-FEB-07	DAY 8 OF TREATMENT
2	07-FEB-07	DAY 8 OF TREATMENT
3	07-FEB-07	DAY 8 OF TREATMENT
4	07-FEB-07	DAY 8 OF TREATMENT

MORTALITY DATA
MALES
GROUP 2 (250 MG/KG)

ANIMAL	SCHEDULED NECROPSY	DAY OF DEATH
5	07-FEB-07	DAY 8 OF TREATMENT
6	07-FEB-07	DAY 8 OF TREATMENT
7	07-FEB-07	DAY 8 OF TREATMENT
8	07-FEB-07	DAY 8 OF TREATMENT

MORTALITY DATA
MALES
GROUP 3 (500 MG/KG)

ANIMAL	SCHEDULED NECROPSY	DAY OF DEATH
9	07-FEB-07	DAY 8 OF TREATMENT
10	07-FEB-07	DAY 8 OF TREATMENT
11	07-FEB-07	DAY 8 OF TREATMENT
12	07-FEB-07	DAY 8 OF TREATMENT

MORTALITY DATA

MALES

GROUP 4 (1000 MG/KG)

ANIMAL	SCHEDULED NECROPSY	DAY OF DEATH
13	07-FEB-07	DAY 8 OF TREATMENT
14	07-FEB-07	DAY 8 OF TREATMENT
15	07-FEB-07	DAY 8 OF TREATMENT
16	07-FEB-07	DAY 8 OF TREATMENT

MORTALITY DATA
FEMALES
GROUP 1 (0 MG/KG)

ANIMAL	SCHEDULED NECROPSY	DAY OF DEATH
17	07-FEB-07	DAY 8 OF TREATMENT
18	07-FEB-07	DAY 8 OF TREATMENT
19	07-FEB-07	DAY 8 OF TREATMENT
20	07-FEB-07	DAY 8 OF TREATMENT

MORTALITY DATA
FEMALES
GROUP 2 (250 MG/KG)

ANIMAL	SCHEDULED NECROPSY	DAY OF DEATH
21	07-FEB-07	DAY 8 OF TREATMENT
22	07-FEB-07	DAY 8 OF TREATMENT
23	07-FEB-07	DAY 8 OF TREATMENT
24	07-FEB-07	DAY 8 OF TREATMENT

MORTALITY DATA
FEMALES
GROUP 3 (500 MG/KG)

ANIMAL	SCHEDULED NECROPSY	DAY OF DEATH
25	07-FEB-07	DAY 8 OF TREATMENT
26	07-FEB-07	DAY 8 OF TREATMENT
27	07-FEB-07	DAY 8 OF TREATMENT
28	07-FEB-07	DAY 8 OF TREATMENT

MORTALITY DATA

FEMALES
GROUP 4 (1000 MG/KG)

ANIMAL	SCHEDULED NECROPSY	DAY OF DEATH
29	07-FEB-07	DAY 8 OF TREATMENT
30	07-FEB-07	DAY 8 OF TREATMENT
31	07-FEB-07	DAY 8 OF TREATMENT
32	07-FEB-07	DAY 8 OF TREATMENT

MACROSCOPICAL FINDINGS
ALL NECROPSIES
MALES
GROUP 1 (0 MG/KG)

ANIMAL 1 (SCHEDULED NECROPSY, 07-FEB-2007)

NO FINDINGS NOTED

ANIMAL 2 (SCHEDULED NECROPSY, 07-FEB-2007)

NO FINDINGS NOTED

ANIMAL 3 (SCHEDULED NECROPSY, 07-FEB-2007)

NO FINDINGS NOTED

ANIMAL 4 (SCHEDULED NECROPSY, 07-FEB-2007)

KIDNEYS .. .. BOTH SIDES: PELVIC DILATION.

MACROSCOPICAL FINDINGS
ALL NECROPSIES
MALES
GROUP 2 (250 MG/KG)

ANIMAL 5 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN.....	ENLARGED.

ANIMAL 6 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN.....	ENLARGED.

ANIMAL 7 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN.....	ENLARGED.

ANIMAL 8 (SCHEDULED NECROPSY, 07-FEB-2007)

LIVER.....	REDUCED IN SIZE.
SPLEEN.....	ENLARGED.

MACROSCOPICAL FINDINGS
ALL NECROPSIES
MALES
GROUP 3 (500 MG/KG)

ANIMAL 9		(SCHEDULED NECROPSY, 07-FEB-2007)
SPLEEN.....	ENLARGED.	
ANIMAL 10		(SCHEDULED NECROPSY, 07-FEB-2007)
SPLEEN.....	ENLARGED.	
ANIMAL 11		(SCHEDULED NECROPSY, 07-FEB-2007)
SPLEEN.....	ENLARGED.	
ANIMAL 12		(SCHEDULED NECROPSY, 07-FEB-2007)
SPLEEN.....	ENLARGED.	

MACROSCOPICAL FINDINGS
ALL NECROPSIES
MALES
GROUP 4 (1000 MG/KG)

ANIMAL 13 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN.....	ENLARGED.
LYMPH NODES.....	INGUINAL: DISCOLORATION, REDDISH.

ANIMAL 14 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN.....	ENLARGED.

ANIMAL 15 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN.....	ENLARGED.
LYMPH NODES.....	INGUINAL: ENLARGED. INGUINAL: DISCOLORATION, REDDISH.

ANIMAL 16 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN.....	ENLARGED.
LYMPH NODES.....	INGUINAL: ENLARGED. INGUINAL: DISCOLORATION, REDDISH.

MACROSCOPICAL FINDINGS
ALL NECROPSIES
FEMALES
GROUP 1 (0 MG/KG)

ANIMAL 17 (SCHEDULED NECROPSY, 07-FEB-2007)

KIDNEYS..... RIGHT SIDE: PELVIC DILATION.

ANIMAL 18 (SCHEDULED NECROPSY, 07-FEB-2007)

NO FINDINGS NOTED

ANIMAL 19 (SCHEDULED NECROPSY, 07-FEB-2007)

NO FINDINGS NOTED

ANIMAL 20 (SCHEDULED NECROPSY, 07-FEB-2007)

NO FINDINGS NOTED

MACROSCOPICAL FINDINGS
ALL NECROPSIES
FEMALES
GROUP 2 (250 MG/KG)

ANIMAL 21 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN.....	ENLARGED.

ANIMAL 22 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN.....	ENLARGED.

ANIMAL 23 (SCHEDULED NECROPSY, 07-FEB-2007)

KIDNEYS.....	BOTH SIDES: PELVIC DILATION.
SPLEEN.....	ENLARGED.

ANIMAL 24 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN.....	ENLARGED.

MACROSCOPICAL FINDINGS
ALL NECROPSIES
FEMALES
GROUP 3 (500 MG/KG)

ANIMAL 25 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN..... ENLARGED.

ANIMAL 26 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN..... ENLARGED.

ANIMAL 27 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN..... ENLARGED.

ANIMAL 28 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN..... ENLARGED.

MACROSCOPICAL FINDINGS
ALL NECROPSIES
FEMALES
GROUP 4 (1000 MG/KG)

ANIMAL 29 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN..... .. .. ENLARGED.

ANIMAL 30 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN..... ENLARGED.

ANIMAL 31 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN..... ENLARGED.

ANIMAL 32 (SCHEDULED NECROPSY, 07-FEB-2007)

SPLEEN..... ENLARGED.

ORGAN WEIGHTS (GRAM)

MALES

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W.	LIVER	KIDNEYS	SPLEEN	TESTES	PROSTATE	EPIDIDYMID	SEMINAL VE
1	342.3	17.08	2.58	0.76	3.23	0.58	0.905	0.77
2	339.6	14.19	2.49	0.71	3.65	0.80	1.180	0.65
3	356 2	14.76	2.54	0.71	3.35	0.89	1.002	1.31
4	359.2	16.82	3.16	0.68	3.58	0.80	1.187	1.56

GROUP 2 (250 MG/KG)

ANIMAL NUMBER	BODY W.	LIVER	KIDNEYS	SPLEEN	TESTES	PROSTATE	EPIDIDYMID	SEMINAL VE
5	338.2	14.23	2.60	2.95	3.43	0.76	0.934	0.92
6	352.8	14.11	2.57	3.08	3.89	0.79	1.092	1.08
7	350.5	14.76	2.50	2.51	4.05	0.71	1.195	1.20
8	320.4	11.21	2.21	1.96	3.54	0.40	1.288	1.92

GROUP 3 (500 MG/KG)

ANIMAL NUMBER	BODY W.	LIVER	KIDNEYS	SPLEEN	TESTES	PROSTATE	EPIDIDYMID	SEMINAL VE
9	326.0	14.82	2.47	3.23	3.42	0.66	1.067	1.27
10	304.7	12.40	2.04	2.48	3.14	0.57	1.162	1.43
11	327.8	15.06	2.66	3.56	3.55	0.80	1.113	1.15
12	318.0	13.64	2.70	3.28	3.69	0.67	1.258	1.46

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W.	LIVER	KIDNEYS	SPLEEN	TESTES	PROSTATE	EPIDIDYMID	SEMINAL VE
13	293.4	12.78	2.82	2.83	3.55	0.56	1.017	0.66
14	300.1	13.13	2.48	3.11	3.66	0.54	1.295	1.53
15	311.6	15.96	2.95	3.43	3.55	0.70	1.070	1.06
16	289.4	12.60	2.30	2.30	3.17	0.46	1.147	1.10

ORGAN/BODY WEIGHT RATIOS (%)
MALES

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	LIVER	KIDNEYS	SPLEEN	TESTES	PROSTATE	EPIDIDYMID	SEMINAL VE
1	342.3	4.99	0.75	0.22	0.94	0.17	0.264	0.22
2	339.6	4.18	0.73	0.21	1.07	0.24	0.348	0.19
3	356.2	4.14	0.71	0.20	0.94	0.25	0.281	0.37
4	359.2	4.68	0.88	0.19	1.00	0.22	0.331	0.43

GROUP 2 (250 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	LIVER	KIDNEYS	SPLEEN	TESTES	PROSTATE	EPIDIDYMID	SEMINAL VE
5	338.2	4.21	0.77	0.87	1.01	0.23	0.276	0.27
6	352.8	4.00	0.73	0.87	1.10	0.22	0.310	0.31
7	350.5	4.21	0.71	0.72	1.15	0.20	0.341	0.34
8	320.4	3.50	0.69	0.61	1.10	0.12	0.402	0.60

GROUP 3 (500 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	LIVER	KIDNEYS	SPLEEN	TESTES	PROSTATE	EPIDIDYMID	SEMINAL VE
9	326.0	4.55	0.76	0.99	1.05	0.20	0.327	0.39
10	304.7	4.07	0.67	0.82	1.03	0.19	0.381	0.47
11	327.8	4.59	0.81	1.08	1.08	0.25	0.340	0.35
12	318.0	4.29	0.85	1.03	1.16	0.21	0.396	0.46

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	LIVER	KIDNEYS	SPLEEN	TESTES	PROSTATE	EPIDIDYMID	SEMINAL VE
13	293.4	4.35	0.96	0.97	1.21	0.19	0.347	0.22
14	300.1	4.37	0.83	1.04	1.22	0.18	0.432	0.51
15	311.6	5.12	0.95	1.10	1.14	0.22	0.344	0.34
16	289.4	4.35	0.80	0.79	1.10	0.16	0.396	0.38

ORGAN WEIGHTS (GRAM)

FEMALES

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W.	LIVER	KIDNEYS	SPLEEN	OVARIES	UTERUS
17	217.7	8.44	1.67	0.60	0.122	0.49
18	208.8	8.42	1.61	0.50	0.115	0.68
19	206.4	9.45	1.93	0.61	0.132	1.22
20	215.1	8.91	1.82	0.49	0.126	1.26

GROUP 2 (250 MG/KG)

ANIMAL NUMBER	BODY W.	LIVER	KIDNEYS	SPLEEN	OVARIES	UTERUS
21	223.6	9.57	1.87	2.13	0.128	1.46
22	205.9	8.29	1.67	2.06	0.088	0.74
23	203.5	8.89	1.75	1.88	0.095	0.67
24	213.2	9.45	1.79	2.82	0.093	1.06

GROUP 3 (500 MG/KG)

ANIMAL NUMBER	BODY W.	LIVER	KIDNEYS	SPLEEN	OVARIES	UTERUS
25	211.5	9.60	1.72	3.04	0.118	0.75
26	209.4	10.33	1.89	2.77	0.107	0.78
27	218.5	10.90	1.88	2.95	0.116	0.61
28	193.7	9.53	1.75	2.31	0.134	0.84

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W.	LIVER	KIDNEYS	SPLEEN	OVARIES	UTERUS
29	196.2	10.36	1.77	2.29	0.130	0.69
30	195.6	9.99	1.65	2.83	0.104	0.71
31	204.6	10.23	1.63	2.80	0.112	1.04
32	195.8	8.89	1.62	2.18	0.109	1.55

ORGAN/BODY WEIGHT RATIOS (%)

FEMALES

GROUP 1 (0 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	LIVER	KIDNEYS	SPLEEN	OVARIES	UTERUS
17	217.7	3.88	0.77	0.28	0.056	0.22
18	208.8	4.03	0.77	0.24	0.055	0.32
19	206.4	4.58	0.94	0.30	0.064	0.59
20	215.1	4.14	0.85	0.23	0.059	0.59

GROUP 2 (250 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	LIVER	KIDNEYS	SPLEEN	OVARIES	UTERUS
21	223.6	4.28	0.84	0.95	0.057	0.65
22	205.9	4.02	0.81	1.00	0.043	0.36
23	203.5	4.37	0.86	0.92	0.047	0.33
24	213.2	4.43	0.84	1.32	0.044	0.50

GROUP 3 (500 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	LIVER	KIDNEYS	SPLEEN	OVARIES	UTERUS
25	211.5	4.54	0.81	1.44	0.056	0.35
26	209.4	4.93	0.90	1.32	0.051	0.37
27	218.5	4.99	0.86	1.35	0.053	0.28
28	193.7	4.92	0.90	1.19	0.069	0.43

GROUP 4 (1000 MG/KG)

ANIMAL NUMBER	BODY W. (GRAM)	LIVER	KIDNEYS	SPLEEN	OVARIES	UTERUS
29	196.2	5.28	0.90	1.17	0.066	0.35
30	195.6	5.11	0.84	1.45	0.053	0.36
31	204.6	5.00	0.80	1.37	0.055	0.51
32	195.8	4.54	0.83	1.11	0.056	0.79

10 ATTACHMENTS

10.1 ATTACHMENT I

CHEMICAL ANALYSIS OF FEED:

- ASSAY FOR CONTAMINANTS

ANALYTICAL TEST REPORT

RCC Study A52885
October 23, 2006

Prepared for	PROVIMI KLIBA AG 4303 Kaiseraugst
Attention of	Dr. Dietmar Ranz
Materials tested	KLIBA-NAFAG 3433 Batch 67/06 of October 10, 2006
Test performed	AAS, GC, GC-MS, HPLC
Test results	See attached Table 1
Submitted	E. Dettwiler
Issued by	K. Biedermann

November 20, 2006/sco

ATTACHMENT

RCC Study A52885
October 23 2006

Table 1 - Test Results

KLIBA-NAFAG 3433
Batch 67/06 of October 10, 2006

PARAMETER	ASSAY LEVEL mg/kg	LIMIT* mg/kg
Aflatoxins (B1, B2, G1, G2), total	< 0.001	0.005
Estrogens (DES, Hexestrol, Dienestrol), total	< 0.001	0.001
Lindane	< 0.005	0.02
Heptachlor	< 0.005	0 02
Malathion	< 0.5	2 5
DDT, total	< 0.025	0 100
Dieldrin	< 0.005	0.02
Cadmium	0.03	0.160
Arsenic	< 0.15	1 0
Lead	< 0.25	1.5
Mercury	< 0.05	0.1
Selenium	< 0.15	0.6
Copper	18	----
PCBs	< 0.025	0.05
Nitrosamines (DMN, DEN, NPIP, NMORPH), total	< 0.002	0.010

< 0 001 = less than 0.001 milligram per kilogram
* = USP EPA, Federal Register, Vol. 44, No. 91, May 9, 1979

10.2 ATTACHMENT II

WATER ANALYSIS:

- BACTERIOLOGICAL AND CHEMICAL ASSAYS, CONTAMINANT ANALYSIS OF DRINKING WATER

BACTERIOLOGICAL ASSAY OF DRINKING WATER, FÜLLINSDORF

Official Laboratory	Liestal, February 08, 2007
Basel-Landschaft	Ref.no. 200054704
Sampling point:	35.991.N Net water RCC Ltd, Füllinsdorf, Bldg. 2
Sampled on:	January 29, 2007
Sample:	
Time of sampling	8.00-8.35
Water temperature (°C)	11.6

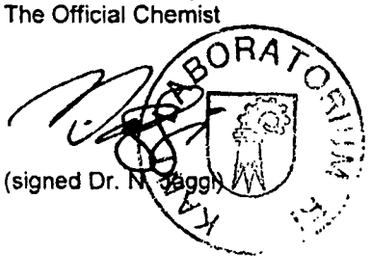
BACTERIOLOGICAL TEST:

Aerobic mesophilic bacteria / ml	1
E.coli / 100 ml	0
Enterococci / 100 ml	0
Coliform Bacteria	0
Clostridium perfringens	0

ASSESSMENT:

At the time of sampling, the tested bacteriological parameters met the requirements for drinking water according to article 275 of the "Eidg. Lebensmittelverordnung".

Official Laboratory
The Official Chemist



(signed Dr. N. Jäggi)

BL070032 Liestal, 13.03.2007

CHEMICAL WATER ANALYSIS, FÜLLINSDORF

Official Laboratory
Basel-Landschaft

Liestal, February 08, 2007
Ref. no. 200054705

Sampling point: 35.991.N, Net water
RCC Ltd, Füllinsdorf, Bldg.2

Sampled on: January 29, 2007

Time of sampling 08.00-08.35

Water temperature (°C) 11.6

CHEMICAL TEST:

Appearance			clear, colourless
Odor			not remarkable
Taste			not remarkable
UV-absorption at 254 nm/100 cm			1.64
Conductivity		µS/cm	571
Oxygen demand	($KMnO_4$ cons.)	mg/l	2.1
Turbidity	FNU		0.06
Chloride	Cl^-	mg/l	18.9
Nitrate	NO_3^-	mg/l	19.2
Sulphate	SO_4^{--}	mg/l	60.4
Nitrite	NO_2^-	mg/l	<0.005
Total hardness		fr.H°	33.1
Alkaline hardness		fr.H°	25.7
Non carbonate hardness		fr.H°	7.4
Calcium	Ca^{++}	mg/l	119.0
Magnesium	Mg^{++}	mg/l	8.2

ASSESSMENT:

At the time of sampling, the tested chemical parameters met the requirements for drinking water according to article 275 of the "Eidg. Lebensmittelverordnung".

Official Laboratory
The Official Chemist

LABORATORIUM

(signed Dr. M. Jäggi)

BL070032 Liestal, 13.03.2007

CONTAMINANT ASSAY OF DRINKING WATER, FÜLLINSDORF

RCC Study No.: B22230

Date of Sampling: January 29, 2007

Sample: H_2O, RCC Ltd, Füllinsdorf, Bldg. 2

PARAMETER	ASSAY LEVEL µg/l	LIMIT * µg/l
Lindane	< 0.05	0.1
Heptachlor	< 0.05	0.1
Malathion	< 0.05	0.1
DDT, total	< 0.05	0.1
Dieldrin	< 0.05	0.1
Cadmium	< 0.5	5
Arsenic	< 3	50
Lead	< 3	50
Mercury	< 1	1
Selenium	< 3	10
Copper	< 4	1500
PCBs (28, 52, 101, 138, 153, 180)	< 0.05	0.1
Nitrosamines, total (DMN, DEN, NPIP, NMORPH)	< 0.05	-----

< 0.05 = less than 0.05 microgram per liter

* Schweizer Lebensmittelbuch

Issued by K. Biedermann

March 12, 2006

10.3 ATTACHMENT III

CERTIFICATES OF ANALYSES OF THE TEST ITEM AND VEHICLE

Honeywell

Specialty Materials
Honeywell
P.O. Box 761
Hopewell, VA 23860

CERTIFICATE OF ANALYSIS

Customer:
RCC Ltd.
Logistics
Zelgliweg 1
CH-4452 Itingen
Switzerland

Product: **METHYL OXIMINO SILANE (OS-1000)**

041201

Attn: Konny Palkner
Phone #: 41 (0) 61 9064 280

	Honeywell Specifications		
Assay, %	90.0	min.	96.1
Early Eluting Compounds, % (before OS-1000)	4.5	max.	2.3
Late Eluting Compounds, % (after OS-1000)	5.0	max.	1.6
Methyl Ethyl Ketoxime, %	0.99	max.	0.59
Color, APHA	40	max.	5
Appearance	Pass		Pass

* Included in early eluting compounds

Date: 12/06/04

Approved: _____
Quality Assurance Department

If you have questions concerning this Certificate of Analysis please contact Karen Crosby, Manager, Quality Assurance, (804) 541-5514 or Ken Nowell, Supervisor, Quality Assurance, (804) 541-5727.

Analysenzertifikat

Carl Roth GmbH + Co · 76185 Karlsruhe
Schoemperlenstraße 1-5
Telefon: 0721 / 56 06-0
Telefax: 0721 / 56 06-149
E-Mail: info@carlroth.de
http://www.carl-roth.de

Datum + Zeichen: 13.06.07 DrHz/

Artikelnummer: 6212
Produkt: Maiskeimöl

Charge: 05566202
Dichte: 0,92
Formel:
Schmelzpunkt:
Flammpunkt:

Reinheit: raffiniert, Ph.Eur.
CAS-Nummer: 8001-30-7
Molekulargewicht:
Lagertemperatur:
Siedepunkt:

Relative Dichte (20°C)	0,919
Brechungsindex n 20/D	1.473
Säurezahl	0,18 mgKOH/g
Peroxidzahl	0,4 meq O_2/kg
Alkalisch reag. Subst.	entspricht
Unverseifbare Anteile	≤2,8%
<C 16:0	≤0,6%
C 16:0 Palmitinsäure	11,1%
C 18:0 Stearinsäure	2%
C 18:1 Ölsäure	32,3%
C 18:2 Linolsäure	52,3%
C 18:3 Linolensäure	0,9%
C 20:0 Arachinsäure	0,5%
C 20:1 Gadoleinsäure	0,3%
C 22:0 Behensäure	0,2%
Sonstige Fettsäure	0,3%

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i.A.

10.4 ATTACHMENT IV

ANALYTICAL PHASE REPORT:

- DETERMINATION OF CONTENT, HOMOGENEITY AND STABILITY OF 2-BUTANONE, O,O',O"-(METHYLSILYLIDYNE) TRIOXIME IN APPLICATION FORMULATIONS

ANALYTICAL PHASE REPORT

Analytical Phase to

2-Butanone, O,O',O"-(methylsilylidyne) trioxime: 7-Day Range-Finding Oral Toxicity (Gavage) Study in the Rat

Subtitle

Determination of Content, Homogeneity and Stability of 2-Butanone, O,O',O"-(methylsilylidyne) trioxime in Application Formulations

Study Director

Dr. R. Gerspach (RCC Ltd, Wölferstrasse 4, Füllinsdorf / Switzerland)

Principal Investigator Analytical Phase

Dr. D. Flade

Completion Date of Analytical Phase Report

October 25, 2007

Test Site

RCC Ltd
Zelgliweg 1
4452 Itingen / Switzerland

RCC Study Number

857737

SIGNATURES

Principal Investigator
Analytical Phase: Dr. D. Flade

D. Flade
.....
Date: October 25, 2007

Management: St. Bär

.....
Date: October 25, 2007

CONTENTS

PREFACE

GENERAL

Analytical Phase to:	2-Butanone, O,O',O"-(methylsilylidyne) trioxime: 7-Day Range-Finding Oral Toxicity (Gavage) Study in the Rat
Sponsor:	SEHSC 11921 Freedom Drive Suite 550 Reston, VA 20190 / USA
Study Director: (Test Facility)	Dr. R. Gerspach RCC Ltd Wölferstrasse 4 4414 Füllinsdorf / Switzerland
Test Site:	RCC Ltd Zelgliweg 1 4452 Itingen / Switzerland

RESPONSIBILITIES

Principal Investigator Analytical Phase:	Dr. D. Flade
Reporting:	R. Martone

SCHEDULE OF ANALYTICAL PHASE

Experimental Starting Date:	March 05, 2007
Experimental Completion Date:	March 06, 2007
Completion Date of Analytical Phase Report:	October 25, 2007

ARCHIVING

RCC Ltd, 4452 Itingen/Switzerland will retain a copy of the study plan, the raw data and the analytical phase report of the present study for at least ten years. No data will be discarded without the sponsor's written consent.

SUMMARY

This analytical phase was conducted at RCC Ltd, Itingen, Switzerland to verify the identity of the test item 2-Butanone, O,O',O"-(methylsilylidyne) trioxime administered and to determine the content, homogeneity and stability of application formulations.

Several application formulations were prepared at the test facility and representative analytical samples were collected and dispatched to the test site internally. The test item concentrations were determined by GC coupled to a FID detector and quantified with the area under the peak.

The identity of 2-Butanone, O,O',O"-(methylsilylidyne) trioxime was confirmed by its retention time which was similar to that measured in the working standards. The test item content in all samples was found to be within the accepted range of ±20% of the nominal content. In addition, the homogenous distribution of 2-Butanone, O,O',O"-(methylsilylidyne) trioxime in dried corn-oil was demonstrated. The application formulations were considered to be stable for at least 7 days when kept under storage conditions.

In conclusion, the results obtained within this phase confirm the correct preparation and storage of application formulations during the conduct of this study.

1 PURPOSE

Within this analytical phase the accurate preparation of application formulations during the study should be verified. For this purpose representative samples had to be analysed for identity of 2-Butanone, O,O',O"-(methylsilylidyne) trioxime, content and homogenous distribution of the test item application formulations. Furthermore, the storage stability of the preparations had to be investigated.

2 MATERIALS AND METHODS

2.1 Test Item

Detailed information concerning the test item is provided in the main Study report. It was also used as an analytical standard.

2.2 Sampling and Storage

Application formulations were prepared for each dose group at the test facility. Representative samples were derived by weighing amounts of 2 g accurately into volumetric glass flasks. Samples for content and homogeneity determination were collected on each occasion from the top, middle and bottom of the mixing beakers. Stability samples were taken from each beaker and kept under storage conditions for 7 days. The time-points samples were dispatched to the test site internally and stored frozen at approximately –20 °C until analysis.

2.3 Reagents and Material

Dichloromethane: Baker no. 9264

2.4 Analytical Procedure

2.4.1 Preparation of Standard Solutions

Stock solutions of 2-Butanone, O,O',O"-(methylsilylidyne) trioxime in dichloromethane were prepared for external standard calibration. For example, 23.96 mg of 2-Butanone, O,O',O"-(methylsilylidyne) trioxime was exactly weighed into a 50 mL volumetric flask and approximately 40 mL of dichloromethane was added. Then, the mixture was sonicated for 5 minutes and the flask was brought to volume with dichloromethane to yield a solution with a concentration of 479.2 µg/mL. Aliquots of this stock standard solution were used to prepare five working standard solutions in dichloromethane with a concentration range from 19.17 to 95.84 µg/mL. Eight standard solutions derived from two stock standard solutions were used for calibration.

2.4.2 Analysis of Samples

The samples received were dissolved in dichloromethane by sonication for 5 minutes and then diluted to volume with dichloromethane. The sample solutions were further diluted with dichloromethane into the calibration range.

2.4.3 High Performance Liquid Chromatographic Determination

GC:	AGILENT 6890
Sampling unit:	AGILENT 7683
Column:	DB 624, 30 m x 0.53 mm, 3 µm film thickness
Carrier gas:	Helium, 4 mL/min, constant flow
Temperatures:	Injector: oven track on (even 3°C higher than oven temperature) Detector: 275 °C Oven: 40 °C for 5 min at 20 °C/min to 240 °C 240 °C for 5 min
Injection:	1 µl, on column
Detector:	FID

2.4.4 Evaluation of Results

Injected samples were quantified by comparing peak areas of 2-Butanone, O,O',O"-(methylsilylidyne) trioxime with reference to the calibration curve. The latter was obtained by correlation of the peak areas of the working standards with their corresponding concentrations (µg/mL), using the linear regression model following equation 1:

$$y = a + b \cdot x \qquad (1)$$

where
y = Response for test item
a = Intercept derived from linear regression of calibration data
b = Slope derived from linear regression of calibration data
x = Actual concentration of test item aliquot

Sample aliquot concentrations were corrected for density of the application formulation and for dilution using the following equation 2:

$$c_{Actual} = \frac{x \cdot V \cdot D}{W \cdot 1000} \qquad (2)$$

where
c_{Actual} = Actual sample concentration [mg/mL]
x = Actual concentration of test item aliquot according to equation 1 [µg/mL]
V = Dilution volume [mL]
W = Sample weight [g]
D = Density of application formulation [0.92 g/mL; as provided by the supplier]

The sample recovery was determined as follows:

$$R = \frac{c_{Actual}}{c_{Nominal}} \cdot 100 \qquad (3)$$

where
R = Sample recovery [%]
c_{Actual} = Actual sample concentration [mg/mL]
$c_{Nominal}$ = Nominal sample concentration [mg/mL]

3 RESULTS

The linearity of the analytical system used for sample analyses was demonstrated with a good relationship between peak areas measured and working standard concentrations. All used calibration points met the acceptance limit of ±20% variation from the calibration curve derived by linear regression analysis. The correlation coefficient calculated was found to be 0.98 and, thus, slightly below the required limit of 0.99 (s. Figure 1).

The 2-Butanone, O,O',O"-(methylsilylidyne) trioxime peak was assigned in sample chromatograms by comparison to that of working standards. In the blank sample chromatogram no peak appeared at the retention time of 2-Butanone, O,O',O"-(methylsilylidyne) trioxime and, therefore, it was confirmed that only dried corn-oil was administered in the control part of the experiment. Examples of chromatograms are shown in Figures 2 and 3.

The application formulations investigated during the study were found to comprise 2-Butanone, O,O',O"-(methylsilylidyne) trioxime in the range from 84.3% to 113.2% and, thus, the required content limit of ±20% with reference to the nominal concentration was met. The homogenous distribution of 2-Butanone, O,O',O"-(methylsilylidyne) trioxime in the preparations is approved because single results found deviate not more than 13.9% (<15%) from the corresponding mean.
In addition, the test item is found to be stable in application formulations when 7 days under storage conditions due to recoveries which met the variation limit of 10% from time-zero (homogeneity) mean.

In conclusion, the results indicate the accurate use of the test item 2-Butanone, O,O',O"-(methylsilylidyne) trioxime and dried corn-oil as vehicle during this study. Application formulations are found to be homogenously prepared and sufficient formulation stability under storage conditions is approved. Detailed results are shown in Table 1.

Table 1: Detailed Results of Application Formulation Analyses
(Rounded results presented are based on calculations with exact data)

Dose Group	Sample taken from/ after	Date of Analysis	Nominal Concentration [mg/mL]	Actual Concentration [mg/mL]	Recovery	Mean Recovery	Maximum Variation from Mean
Date of Preparation: 31-Jan-2007							
1	vehicle	05-Mar-07	0.000	0.000	—	—	—
2	top	05-Mar-07	125.0	105.3	84.3%	86.4%	3.8%
	middle	05-Mar-07	125.0	106.6	85.3%		
	bottom	05-Mar-07	125.0	112.0	89.6%		
	7 days *	05-Mar-07	125.0	118.2	94.6%	—	9.5%
3	top	05-Mar-07	250.0	230.0	92.0%	95.1%	3.5%
	middle	05-Mar-07	250.0	237.1	94.8%		
	bottom	05-Mar-07	250.0	246.2	98.5%		
	7 days *	05-Mar-07	250.0	234.4	93.8%	—	1.4%
4	top	05-Mar-07	500.0	444.7	88.9%	99.4%	13.9%
	middle	05-Mar-07	500.0	565.9	113.2%		
	bottom	05-Mar-07	500.0	480.3	96.1%		
	7 days *	05-Mar-07	500.0	475.3	95.1%	—	4.4%

* under storage conditions

Figure 1: Calibration Curve

Standard Concentration [µg/mL]	Peak Area [counts]	Variation of Peak Area
19.17	117.24	-0.9%
38.34	230.41	-14.3%
57.50	359.35	-13.6%
76.67	515.40	-7.3%
95.84	733.94	4.9%
18.67	130.77	12.4%
37.34	278.02	8.0%
56.02	434.84	8.7%
74.69	563.71	4.5%
93.63	663.77	-2.6%

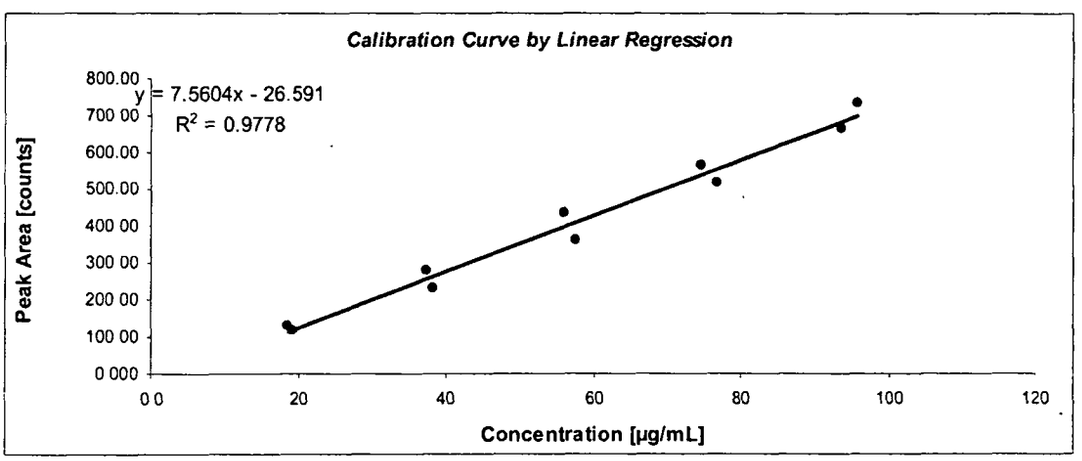
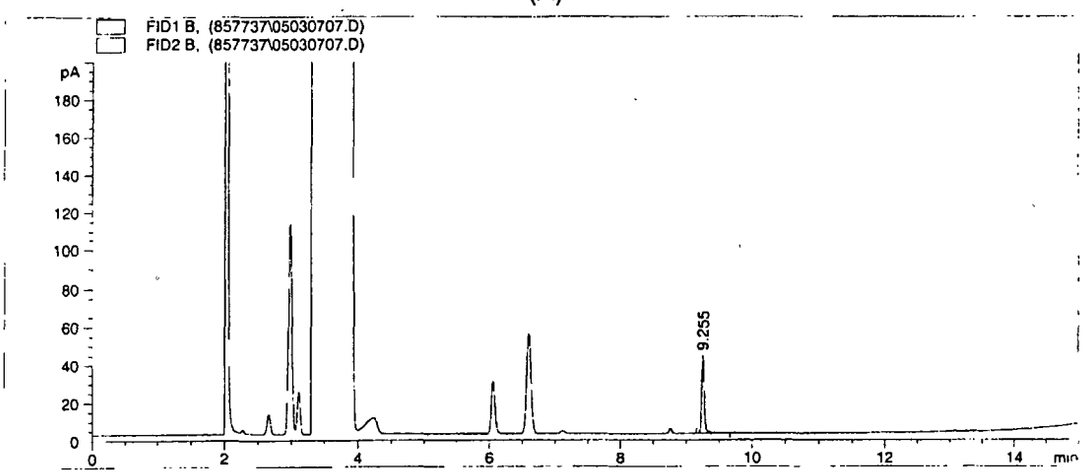


Figure 2: GC-Chromatograms of Standard Solutions
(A) Standard solution: 19.17 µg/mL
(B) Standard solution: 95.84 µg/mL

(A)



(B)

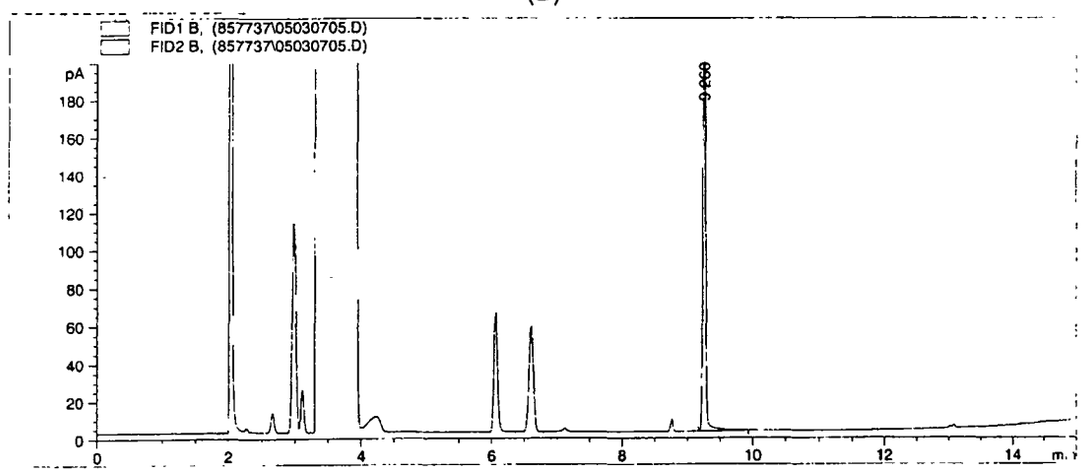
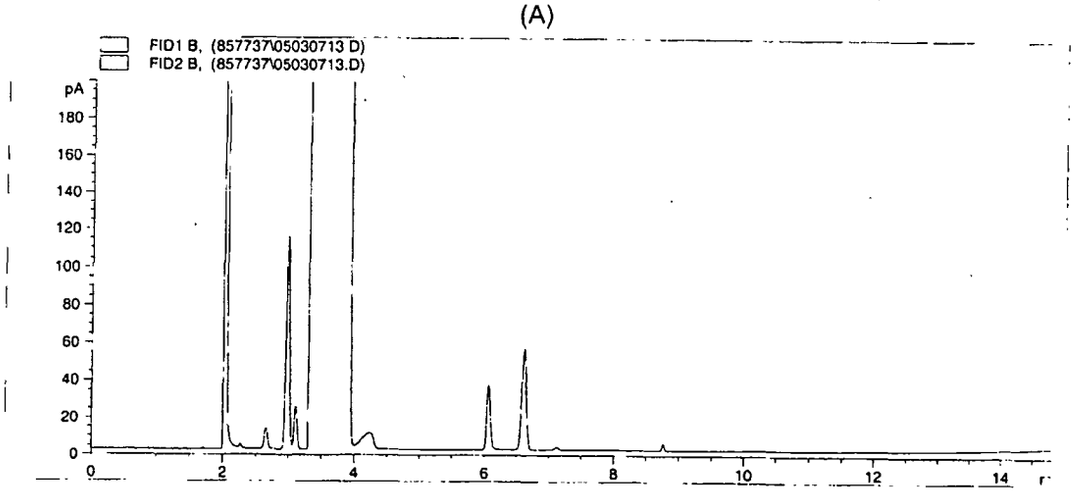


Figure 3: GC-Chromatograms of Test Samples
(A) Dose group 1, control sample, approx. 2500 x diluted
(B) Dose group 2 (top), nominal concentration: 125.0 mg/mL, approx. 2500 x diluted

(A)



(B)

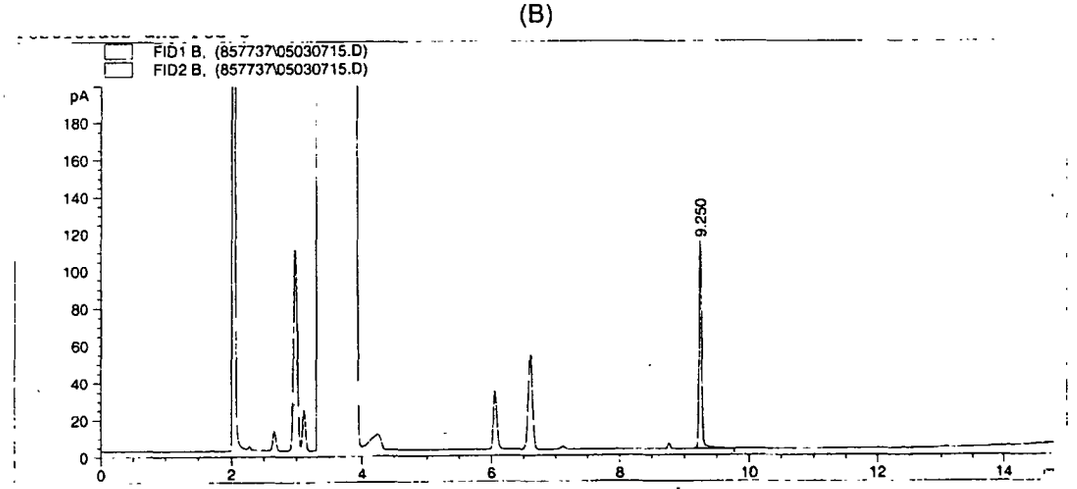


Figure 3: Continued

(C) Dose group 4 (top), nominal concentration: 500.0 mg/mL, approx. 10000 x diluted

(C)